Access D: _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: _____ Examiner # :_____ Date: _____
Art Unit: _____ Phone Number 30_____ Serial Number: _____
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

****

STAFF USE ONLY

Searcher: _____ of Contact: Sheppard
Searcher Phone #: _____
Searcher Location: ~~Tel: 308-4499~~
Date Searcher Picked Up: _____
Date Completed: 6/3/01
Searcher Prep & Review Time: _____
Clerical Prep Time: _____
Online Time: _____

Type of Search

NA Sequence (#)_____
AA Sequence (#)_____
Structure (#) _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN _____
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis_____
Sequence Systems _____
WWW/Internet _____
Other (specify)_____

PTO-1590 (1-2000)

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OM of: US-09-526-193A-1_COPY_1_60 to: EST:*   out_format : pfs

Date: Jun 2, 2001  7:52 PM

About: Results were produced by the GenCore software, version 4.5,
       Copyright (c) 1993-2000 Compugen Ltd.

Command line parameters:
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 -MINMATCH=0.100 -LOOPCL=0.000 -LOOPEXT=0.000 -QGAPOP=4.500
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 -FGAPEXT=7.000 -YGAPOP=10.000 -YGAPEXT=0.500 -DELOP=6.000
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Search information block:
Query: US-09-526-193A-1_COPY_1_60
Query length: 60
Database: EST:*
Database sequences: 9623517
Database length: 73081774
Search time (sec): 1122.300000


score_list:
Sequence                Strd Orig    ZScore    EScore Len   ! Documentation  ..
gb_est30:AU135588         +  334.00  737.13   5.8e-32   736  ! AU135588 AU135588 PLACE1 Homo s
gb_est44:AW313960         +  227.00  503.47   6.0e-19   335  ! AW313960 9668 MARC 2PIG Sus scr
gb_est91:BF721262         +  213.00  472.50   3.2e-17   315  ! BF721262 mab64g11.y1 Soares_thy
gb_est87:BF455614         -  150.00  332.96   1.9e-09   243  ! BF455614 UI-M-CG0p-biq-d-02-0-U
gb_gss32:CNS05RRH         -  105.50  218.37   0.0045    1065  ! AL350918 Tetraodon nigroviridi
gb_est88:BF495663         +  100.00  211.46   0.0110    603  ! BF495663 AT04622.5prime AT Dros
gb_gss31:CNS04053         +   96.50  199.06   0.0538    962  ! AL268464 Tetraodon nigroviridis
gb_gss30:CNS01Y8B         +   88.50  182.55   0.4471    821  ! AL172676 Tetraodon nigroviridis
gb_est41:AW106575         +   85.50  178.42   0.7595    625  ! AW106575 um29h03.y1 Sugano mous
gb_gss31:CNS03SGV         +   84.00  172.38   1.65      823  ! AL258520 Tetraodon nigroviridis
gb_gss27:B29539           -   78.00  162.67   5.72      554  ! B29539 T10K17TFB TAMU Arabidops
gb_est17:AI220973         +   76.00  159.59   8.50      478  ! AI220973 qg04a04.x1 Soares_plac
gb_est16:AI149299         +   76.00  158.96   9.21      510  ! AI149299 qc72c12.x1 Soares_plac
gb_gss29:CNS008DW         -   75.50  151.72   23.32     961  ! AL052459 Drosophila melanogaste
gb_est87:BF442774         +   75.00  158.42   9.87      427  ! BF442774 260029 MARC 2PIG Sus s
gb_est47:AW494916         +   75.00  155.77   13.87     562  ! AW494916 UI-M-BH3-auq-b-01-0-UI
gb_est19:AI402861         +   74.00  154.67   15.98     499  ! AI402861 GH22184.5prime GH Dros
gb_est21:AI516568         +   74.00  153.92   17.59     539  ! AI516568 LD42471.5prime LD Dros
gb_est41:AW105861         +   74.00  153.23   19.22     579  ! AW105861 ul94g12.y1 Sugano mous
gb_est14:AA941543         +   74.00  151.02   25.51     728  ! AA941543 LD25731.5prime LD Dros
gb_est42:AW153316         +   73.50  150.41   27.59     690  ! AW153316 fi19c07.y1 Sugano Kawa
gb_est2:AA098718          -   73.00  155.62   14.15     358  ! AA098718 T4048 MVAT4 bloodstrea
gb_gss27:B43728           -   72.00  152.29   21.68     400  ! B43728 HS-1058-A2-A05-MR.abi CI
gb_est7:AA422007          +   72.00  150.61   26.89     476  ! AA422007 zv31c04.s1 Soares ovar
gb_gss33:TA94B12Q         -   72.00  148.72   34.26     579  ! AL465384 T. brucei sheared genc
gb_est57:BB152328         +   71.00  155.05   15.22     238  ! BB152328 BB152328 RIKEN full-le
gb_est48:AW571050         +   71.00  150.38   27.70     386  ! AW571050 ra15f04.y1 Bird-Rao Me
gb_est80:BE944442         -   71.00  150.23   28.23     392  ! BE944442 UI-M-BH3-awe-h-12-0-UI
gb_est102:R43911          -   71.00  148.04   37.40     492  ! R43911 yg22a05.s1 Soares infant
gb_est79:BE823385         +   71.00  145.92   49.10     613  ! BE823385 GM700019B10H5 Gm-r1070
gb_est55:BB068678         +   70.50  152.08   22.27     288  ! BB068678 BB068678 RIKEN full-le
gb_est7:AA412619          -   70.50  147.54   39.87     461  ! AA412619 zt97b09.r1 Soares_test
gb_est42:AW120216         +   70.50  146.14   47.72     533  ! AW120216 614086G06.y1 614 - roc
gb_gss29:CNS00VX1         -   70.00  151.40   24.31     275  ! AL092851 Arabidopsis thaliana g
gb_gss27:B26572           -   70.00  147.52   39.97     411  ! B26572 T10I5TF TAMU Arabidopsis
gb_est22:AI568925         +   70.00  146.69   44.47     448  ! AI568925 tq71e05.x1 NCI_CGAP_Lu
gb_est103:T22465          -   70.00  146.10   47.94     476  ! T22465 4473 Lambda-PRL2 Arabido
gb_est24:AI743770         +   70.00  144.74   57.07     548  ! AI743770 wg53f11.x1 Soares_NSF_
gb_est82:BF061307         +   70.00  144.21   61.09     579  ! BF061307 7i77e06.x1 NCI_CGAP_Ov
gb_est87:BF448717         +   70.00  143.07   70.77     652  ! BF448717 7n93f02.x1 NCI_CGAP_Ov
gb_est96:BG129702         -   69.50  142.06   80.54     644  ! BG129702 EST475348 tomato shoot
gb_gss3:AQ208984          +   69.00  144.65   57.75     438  ! AQ208984 HS_3230_A2_H07_MR C
gb_est90:BF641501         +   69.00  143.67   65.51     485  ! BF641501 NF066B04IN1F1032 In
gb_gss30:CNS02T3F         +   69.00  136.52   163.85    1017  ! AL212676 Tetraodon nigrovir
gb_gss31:CNS03KKG         +   69.00  135.71   181.78    1106  ! AL248281 Tetraodon nigrovir

seq_name: gb_est30:AU135588

seq_documentation_block:
LOCUS       AU135588      736 bp    mRNA            EST       24-OCT-2000
DEFINITION  AU135588 PLACE1 Homo sapiens cDNA clone PLACE1002437 5', mRNA
            sequence.
ACCESSION   AU135588
VERSION     AU135588.1  GI:10996127
KEYWORDS    EST.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 736)
  AUTHORS   Ota,T., Nishikawa,T., Suzuki,Y., Ishii,S., Saito,K., Kawai,Y.,
            Yamamoto,J., Wakamatsu,A., Nakamura,Y., Nagai,T., Sugano,S. and
            Isogai,T.
  TITLE     HRI human cDNA project
  JOURNAL   Unpublished (2000)
COMMENT     Contact: Takao Isogai
            Genomics Laboratory
            Helix Research Institute
            1532-3 Yana, Kisarazu, Chiba 292-0812, Japan
            Tel: 81-438-52-3951
            Fax: 81-438-52-3952
            Email: genomics@hri.co.jp
            HRI human cDNA project; 5'- & 3'-end one pass sequencing: Helix
            Research Institute; cDNA library construction: Department of
            Virology, Institute of Medical Science, University of Tokyo, and
            Helix Research Institute.
FEATURES             Location/Qualifiers
     source          1. .736
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="PLACE1002437"
                     /clone_lib="PLACE1"
                     /tissue_type="placenta"
                     /note="Vector: pME18SFL3"
BASE COUNT      163 a    199 c    199 g    170 t      5 others
ORIGIN


alignment_scores:
           Quality:  334.00              Length:     60
             Ratio:  5.567                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-526-193A-1_COPY_1_60 x AU135588   ..

 Align seg 1/1  to: AU135588  from: 1  to: 736

       1 MetAlaCysTrpProGlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPh 17
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     314 ATGGCTTGTTGGCCCCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 363

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     364 CAGAAGAAGACAAACATGTCAGCTGCTGCTGGAAGTGGCCTGGCCTCTAT 413

      34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     414 TTATCTTCCTGATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAA 463

      51 GlnHisGluCysHisPheProAsnLysAla 60
         ||||||||||||||||||||||||||||||
     464 CAACATGAATGCCATTTTCCAAATAAAGCC 493
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seq_name: gb_est44:AW313960

seq_documentation_block:
LOCUS       AW313960      335 bp    mRNA            EST       09-JUL-2000
DEFINITION  9668 MARC 2PIG Sus scrofa cDNA 5', mRNA sequence.
ACCESSION   AW313960
VERSION     AW313960.1  GI:6743216
KEYWORDS    EST.
SOURCE      pig.
  ORGANISM  Sus scrofa
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
REFERENCE   1  (bases 1 to 335)
  AUTHORS   Fahrenkrug,S.C., Freking,B.A., Rohrer,G.A., Smith,T.P.L., Casas,E.,
            Stone,R.T., Heaton,M.P., Grosse,W.M., Bennett,G.A., Laegreid,W.W.
            and Keele,J.W.
  TITLE     Design and use of two pooled tissue normalized cDNA libraries for
            EST discovery in swine
  JOURNAL   Unpublished (2000)
COMMENT     Contact: Smith TPL
            USDA, ARS, US Meat Animal Research Center
            PO Box 166, Clay Center, NE 68933-0166, USA
            Tel: 402 762 4366
            Fax: 402 762 4390
            Email: smith@email.marc.usda.gov
            Single pass sequencing. Bases called and trimmed with phred
            v0.980904.e. Vector identified by cross_match with the -minscore 20
            and -minmatch 12 options.
            PCR PRimers
            FORWARD: AGGAAACAGCTATGACCAT
            BACKWARD: GTTTTCCCAGTCACGACG
            Plate: 8  row: F  column: 18
            Seq primer: ATTTAGGTGACACTATAG.
FEATURES             Location/Qualifiers
     source          1. .335
                     /organism="Sus scrofa"
                     /db_xref="taxon:9823"
                     /clone_lib="MARC 2PIG"
                     /tissue_type="pooled"
                     /lab_host="DH10B"
                     /note="Vector: pCMV SPORT6; Site_1: XbaI; Site_2: XhoI;
                     Library made from pooled tissue from testis, ovary,
                     endometrium, hypothalamus, pituitary, and placenta."
BASE COUNT       61 a    107 c     84 g     83 t
ORIGIN


alignment_scores:
            Quality:  227.00            Length:     59
              Ratio:  4.633               Gaps:      0
 Percent Similarity:  83.051   Percent Identity: 67.797

alignment_block:
 US-09-526-193A-1_COPY_1_60 x AW313960   ..

 Align seg 1/1  to: AW313960  from: 1  to: 335

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         ||||||   |||   ||||||   ||||||||||||||||||:::   ::
     125 ATGGCCTTCTGGACACAGCTAATGCTGCTGCTTTGGAAGAATTTCCTGTA 174

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         :|||||||||||||       |||||||||:::|||:::   ||||||||||
     175 TCGCAGGAGACAGCCGATCCAGCTCTTGGTGGAGTTGATGTGGCCTCTCT 224

      34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
         ||:::|||:::||||||:::::|||||   |||:::||||||  |||
     225 TTCTCTTCTTCATTCTGGTGGCGGTCCGCCATTCCCACCCCCCACTCGAG 274

      51 GlnHisGluCysHisPheProAsnLys 59
         ||||||||||||||||   ||||||
     275 CAGCATGAATGCCACTTCTCCAACAAG 301
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seq_name: gb_est91:BF721262

seq_documentation_block:
LOCUS       BF721262      315 bp    mRNA            EST       03-JAN-2001
DEFINITION  mab64g11.y1 Soares_thymus_2NbMT Mus musculus cDNA clone
            IMAGE:3975356 5' similar to SW:ABCR_HUMAN P78363 RETINAL-SPECIFIC
            ATP-BINDING CASSETTE TRANSPORTER ;, mRNA sequence.
ACCESSION   BF721262
VERSION     BF721262.1  GI:12022264
KEYWORDS    EST.
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 315)
  AUTHORS   NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap.
  TITLE     National Cancer Institute, Cancer Genome Anatomy Project (CGAP),
            Tumor Gene Index
  JOURNAL   Unpublished (1997)
COMMENT     Contact: Robert Strausberg, Ph.D.
            Tel: (301) 496-1550
            Email: Robert_Strausberg@nih.gov
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            MGI:1475388
            Seq primer: -40RP from Gibco
            High quality sequence stop: 288.
FEATURES             Location/Qualifiers
     source          1. .315
                     /organism="Mus musculus"
                     /strain="C57BL/6J"
                     /db_xref="taxon:10090"
                     /clone="IMAGE:3975356"
                     /clone_lib="Soares_thymus_2NbMT"
                     /sex="male"
                     /tissue_type="Thymus"
                     /dev_stage="4 weeks"
                     /lab_host="DH10B"
                     /note="Vector: pT7T3D-Pac (Pharmacia) with a modified
                     polylinker; Site_1: Not I; Site_2: Eco RI; 1st strand cDNA
                     was primed with a Not I - oligo(dT) primer [5'
                     TGTTACCAATCTGAAGTGGGAGCGGCCGCGTTTTTTTTTTTTTTTTTTTTTTT
                     3']; double-stranded cDNA was ligated to Eco RI adaptors
                     (Pharmacia), digested with Not I and cloned into the Not I
                     and Eco RI sites of the modified pT7T3 vector. RNA
                     provided by Dr. Bertrand Jordan. Library went through two
                     rounds of normalization, and was constructed by Bento
                     Soares and M.Fatima Bonaldo."
BASE COUNT       66 a    105 c     69 g     75 t
ORIGIN


alignment_scores:
            Quality:  213.00            Length:     53
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 Percent Similarity:  86.792   Percent Identity: 69.811

alignment_block:
 US-09-526-193A-1_COPY_1_60 x BF721262   ..

 Align seg 1/1  to: BF721262  from: 1  to: 315

       7 LeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGlnThrCy 23
         |||   ||||||||||||||||||   |||:::||||||||||||
       1 CTGATGCTTCTGCTGTGGAAAAATTACACCTATCGACGGAGACAACCGAT 50

      23 sGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleLeuI 40
         ||||||||||:::|||:::   ||||||||||:::|||:::|||||||:
      51 CCAACTACTAGTGGAGTTGCTTTGGCCCCTCTTCCTCTTCTTCATCCTAG 100

      40 leSerValArgLeuSerTyrProProTyrGluGlnHisGluCysHisPhe 56
         :::::||||||   |||:::||||||   |||:::|||||||||||||||
     101 TGGCTGTCCGTCACTCCCACCCCCCTCTGGAGCATCACGAATGCCACTTT 150
```

```
     57 ProAsnLys 59
        |||||||||
    151 CCAAACAAG 159

seq_name: gb_est87:BF455614

seq_documentation_block:
LOCUS       BF455614      243 bp    mRNA            EST       01-DEC-2000
DEFINITION  UI-M-CG0p-biq-d-02-0-UI.s1 NIH_BMAP_Ret4_S2 Mus musculus cDNA clone
            UI-M-CG0p-biq-d-02-0-UI 3', mRNA sequence.
ACCESSION   BF455614
VERSION     BF455614.1  GI:11521783
KEYWORDS    EST.
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 243)
  AUTHORS   Bonaldo,M.F., Lennon,G. and Soares,M.B.
  TITLE     Normalization and subtraction: two approaches to facilitate gene
            discovery
  JOURNAL   Genome Res. 6 (9), 791-806 (1996)
  MEDLINE   97044477
COMMENT     Contact: Chin, H
            National Institute of Mental Health
            6001 Executive Blvd. Room 7N-7190, MSC 9643, Bethesda, MD
            20892-9643, USA
            Tel: 301 443 1706
            Fax: 301 443 9890
            Email: mEST@mail.nih.gov
            The sequence contained an oligo-dT track that was present in the
            oligonucleotide that was used to prime the synthesis of first
            strand cDNA and therefore this may represent a bonafide poly A
            tail. The sequence tag present in the cDNA between the NotI site
            and the oligo-dT track served to identify it as a clone from the
            retina tissue cDNA Library Preparation: M.B. Soares Lab Clone
            distribution: Researchers may obtain BMAP cDNA clones from RESEARCH
            GENETICS. It should be noted that Bento Soares is generating a
            small number of additional specialized non-redundant arrays of BMAP
            cDNAs whose availability will be considered under appropriate and
            limited collaborative arrangements
            Seq primer: M13 Forward
            POLYA=Yes.
FEATURES             Location/Qualifiers
     source          1. .243
                     /organism="Mus musculus"
                     /strain="C57BL/6J"
                     /db_xref="taxon:10090"
                     /clone="UI-M-CG0p-biq-d-02-0-UI"
                     /clone_lib="NIH_BMAP_Ret4_S2"
                     /lab_host="DH10B (Life Technologies)"
                     /note="Vector: pT7T3D-Pac (Pharmacia) with a modified
                     polylinker; Site_1: Not I; Site_2: Eco RI; The
                     NIH_BMAP_Ret4_S2 library is a subtracted library,
                     ultimately derived from mouse retina tissue libraries at
                     various stages of development. For a detailed description
                     of the library from which this clone was derived, please
                     visit our web site at brainest.eng.uiowa.edu.
                     TAG_LIB=NIH_BMAP_Ret4_S2
                     TAG_TISSUE=adult-retina
                     TAG_SEQ=GTCAGCGCGCAC"
BASE COUNT       68 a     68 c     51 g     56 t
ORIGIN


alignment_scores:
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              Ratio:  3.409                Gaps:      0
 Percent Similarity:  81.481   Percent Identity: 50.000

alignment_block:
 US-09-526-193A-1_COPY_1_60 x BF455614/rev   ..
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 Align seg 1/1  to reverse of: BF455614  from: 1  to: 243

       6 GlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGlnTh 22
         |||::::::|||||||||||||||||||   |||:::|||:::||||||
     163 CAGATACAGCTTTTGCTTTGGAAGAACTGGACTCTGAGGAAAAGGCAGAA 114

      22 rCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleL 39
            :::::::::::|||::::::|||||||||   :::||||||:::|
     113 GATTCGCTTTGTAGTGGAACTCGTGTGGCCTTTGTCTTTGTTTTTGGTGT 64

      39 euIleSerValArgLeuSerTyrProProTyrGluGlnHisGluCysHis 55
         |||||   :::|||   :::   |||   |||:::||||||||||||:::
      63 TAATCTGGCTGAGGAATGCCAACCCACTCTATAGTCAGCATGAATGCCAA 14

      56 PheProAsnLys 59
            :::|||
      13 AAAAAAAAAAAA 2

seq_name: gb_gss32:CNS05RRH

seq_documentation_block:
LOCUS       CNS05RRH     1065 bp    DNA             GSS       26-MAY-2000
DEFINITION  Tetraodon nigroviridis genome survey sequence T3 end of clone
            031H21 of library A from Tetraodon nigroviridis, genomic survey
            sequence.
ACCESSION   AL350918
VERSION     AL350918.1  GI:8244688
KEYWORDS    GSS; genome survey sequence.
SOURCE      Tetraodon nigroviridis.
  ORGANISM  Tetraodon nigroviridis
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
            Eurypterygii; Ctenosquamata; Acanthomorpha; Euacanthomorpha;
            Holacanthopterygii; Acanthopterygii; Percomorpha;
            Tetraodontiformes; Tetraodontoidei; Tetraodontidae; Tetraodon.
REFERENCE   1  (bases 1 to 1065)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Fizames,C., Fisher,C.,
            Bouneau,L., Billault,A., Quetier,F., Saurin,W., Bernot,A. and
            Weissenbach,J.
  TITLE     Charaterization and repeat analysis of the compact genome of the
            freshwater pufferfish Tetraodon nigroviridis
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 1065)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Bouneau,L., Fisher,C.,
            Bernot,A., Fizames,C., Wincker,P., Brottier,P., Quetier,F.,
            Saurin,W. and Weissenbach,J.
  TITLE     Human gene number estimate provided by genome wide analysis using
            Tetraodon nigroviridis DNA sequence
  JOURNAL   Unpublished
REFERENCE   3  (bases 1 to 1065)
  AUTHORS   Genoscope.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-APR-2000) to the EMBL/GenBank/DDBJ databases
COMMENT     This sequence is a single read and was generated as part of a large
            scale clone-end sequencing project of the Tetraodon nigroviridis
            genome. For more information, please take a look at
            http://www.genoscope.cns.fr/Tetraodon.
FEATURES             Location/Qualifiers
     source          1. .1065
                     /organism="Tetraodon nigroviridis"
                     /db_xref="taxon:99883"
                     /clone="031H21"
                     /clone_lib="A"
                     /note="Genoscope sequence ID : C0AA031CD11A1-end : T3"
BASE COUNT      262 a    277 c    290 g    202 t     34 others
ORIGIN


alignment_scores:
            Quality:  105.50              Length:     82
              Ratio:  2.705                Gaps:      1
 Percent Similarity:  47.561   Percent Identity: 32.927
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alignment_block:
 US-09-526-193A-1_COPY_1_60 x CNS05RRH/rev   ..

 Align seg 1/1  to reverse of: CNS05RRH  from: 1  to: 1065

       6 GlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGln.. 21
         |||:::|||||||||||||||||||||||   |||:::|||||||||||||
     791 CAAATCCGCCTTTTGCTGTGGAAGAACTGGACTCTGCGGAGGAGACAGAA 742

      21 ............................................... 21

     741 GGTATTCAGGCCGGCACGCCAGGACAGGGTGGTTAGCAGGCAACCGTCCG 692

      22 .............................................Thr 22

     691 CCTGTTTCGGGAGGAAGGTTTGTGTCGGACTGAACTCTTCCTCGTCCAGG 642

      23 CysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleLe 39
         |||   :::::::::|||:::   |||||||||:::::|||      ||
     641 TGCGT.TTCTTTGTGGAGATCTTCTGGCCGTTGCTGCTCTTCAGCGGTCT 593

      39 uIleSerValArgLeuSerTyrProProTyrGluGlnHisGluCys 54
         |:::   :::|||   :::   |||   |||:::||||||||||||
     592 GGTGTGGCTCAGGAAGGCCAACCCGCTGTACCAACAACATGAGTGT 547

seq_name: gb_est88:BF495663

seq_documentation_block:
LOCUS       BF495663      603 bp    mRNA            EST       06-DEC-2000
DEFINITION  AT04622.5prime AT Drosophila melanogaster adult testes pOTB7
            Drosophila melanogaster cDNA clone AT04622 5, mRNA sequence.
ACCESSION   BF495663
VERSION     BF495663.1  GI:11578964
KEYWORDS    EST.
SOURCE      fruit fly.
  ORGANISM  Drosophila melanogaster
            Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
            Pterygota; Neoptera; Endopterygota; Diptera; Brachycera;
            Muscomorpha; Ephydroidea; Drosophilidae; Drosophila.
REFERENCE   1  (bases 1 to 603)
  AUTHORS   Stapleton,M., Brokstein,P., Hong,L., Agbayani,A., Baxter,E., Berman
            ,B., Carlson,J., Champe,M., Chavez,C., Chew,M., Dorsett,V., Farfan
            ,D., Frise,E., George,R., Gonzalez,M., Guarin,H., Harris,N., Li,P.,
            Liao,G., Miranda,A., Misra,S., Mungall,C.J., Nunoo,J., Pacleb,J.,
            Park,S., Paragas,V., Phouanenavong,S., Wan,K., Yu,C., Celniker,S.,
            Lewis,S.E. and Rubin,G.M.
  TITLE     Berkeley Drosophila Gene Collection Project
  JOURNAL   Unpublished (2000)
COMMENT     Contact: Stapleton, M.
            BDGP
            Lawrence Berkeley National Lab
            One Cyclotron Rd, Berkeley, CA 94720, USA
            Fax: 510 486 6798
            Email: http://www.fruitfly.org/EST, est@fruitfly.berkeley.edu
            hit genomic sequence AE003569
            Plate: AT.46  row: B  column: 10
            High quality sequence stop: 596.
FEATURES             Location/Qualifiers
     source          1. .603
                     /organism="Drosophila melanogaster"
                     /db_xref="taxon:7227"
                     /clone="AT04622"
                     /clone_lib="AT Drosophila melanogaster adult testes pOTB7"
                     /sex="male"
                     /dev_stage="0-3 day old Ore-R males"
                     /lab_host="DH5-alpha or DH5-alpha TonA as per database (AT
                     121 on are in Tona cells)"
                     /note="Organ: ADULT testes; Vector: pOTB7; Site_1: EcoRI;
                     Site_2: XhoI; The mRNA for the testis library was made
                     from testes and seminal vessicles hand dissected from 0-3
                     day old Ore-R males. RNA kindly provided by the lab of
                     Margaret Fuller. Sized fractionated cDNAs were directly
                     ligated into pOTB7. Plasmid cDNA library."
BASE COUNT      140 a    149 c    168 g    146 t
ORIGIN


alignment_scores:
            Quality:  100.00            Length:     54
              Ratio:  2.703               Gaps:      0
 Percent Similarity:  68.519   Percent Identity: 37.037

alignment_block:
 US-09-526-193A-1_COPY_1_60 x BF495663   ..

 Align seg 1/1  to: BF495663  from: 1  to: 603

       6 GlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGlnTh 22
         :::::::|||   ||||||   |||:::|||      |||   ||||||
     240 GAGGTCCGGGAGCTGTTGCGAAAGGATTTGCTGGTGCGATGGCGACAGAA 289

      22 rCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleL 39
               |||:::   :::||||||||||:::::::::|||::::::|
     290 AGGGCTGAGTCTGATCCTGTTGGCCTGGCCAGTGATGGTCTTTATGCTGC 339

      39 euIleSerValArgLeuSerTyrProProTyrGluGlnHisGluCysHis 55
         ||      :::|||||||:::|||         |||   :::   |||:::
     340 TCTATCTGATCCGTCTGAAGTACGGATCGGAGGAGTTGGAGGCCTGCCAG 389

      56 PheProAsnLys 59
         :::|||::::::
     390 TATCCCACTCGC 401

seq_name: gb_gss31:CNS04053

seq_documentation_block:
LOCUS       CNS04053      962 bp    DNA             GSS       18-MAY-2000
DEFINITION  Tetraodon nigroviridis genome survey sequence T7 end of clone
            071B16 of library G from Tetraodon nigroviridis, genomic survey
            sequence.
ACCESSION   AL268464
VERSION     AL268464.1  GI:7990313
KEYWORDS    GSS; genome survey sequence.
SOURCE      Tetraodon nigroviridis.
  ORGANISM  Tetraodon nigroviridis
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
            Eurypterygii; Ctenosquamata; Acanthomorpha; Euacanthomorpha;
            Holacanthopterygii; Acanthopterygii; Percomorpha;
            Tetraodontiformes; Tetraodontoidei; Tetraodontidae; Tetraodon.
REFERENCE   1  (bases 1 to 962)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Fizames,C., Fisher,C.,
            Bouneau,L., Billault,A., Quetier,F., Saurin,W., Bernot,A. and
            Weissenbach,J.
  TITLE     Charaterization and repeat analysis of the compact genome of the
            freshwater pufferfish Tetraodon nigroviridis
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 962)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Bouneau,L., Fisher,C.,
            Bernot,A., Fizames,C., Wincker,P., Brottier,P., Quetier,F.,
            Saurin,W. and Weissenbach,J.
  TITLE     Human gene number estimate provided by genome wide analysis using
            Tetraodon nigroviridis DNA sequence
  JOURNAL   Unpublished
REFERENCE   3  (bases 1 to 962)
  AUTHORS   Genoscope.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-APR-2000) to the EMBL/GenBank/DDBJ databases
COMMENT     This sequence is a single read and was generated as part of a large
            scale clone-end sequencing project of the Tetraodon nigroviridis
            genome. For more information, please take a look at
            http://www.genoscope.cns.fr/Tetraodon.
FEATURES             Location/Qualifiers
     source          1. .962
                     /organism="Tetraodon nigroviridis"
```

```
                     /db_xref="taxon:99883"
                     /clone="071B16"
                     /clone_lib="G"
                     /note="Genoscope sequence ID : C0BG071DA08LP1-end : T7"
BASE COUNT      186 a    257 c    234 g    279 t      6 others
ORIGIN


alignment_scores:
            Quality:   96.50             Length:     96
              Ratio:  2.539               Gaps:      3
 Percent Similarity:  39.583   Percent Identity: 26.042

alignment_block:
 US-09-526-193A-1_COPY_1_60 x CNS04053   ..

 Align seg 1/1  to: CNS04053  from: 1  to: 962

      12 TrpLys.............................AsnLeuThrPheAr 18
         ||||||                            :::|||   |||||
       1 TGGAAACCAGGACAGGGTGGTTAGCAGGCAACCGTACGCCTCCTGTTTCG 50

      18 gArgArgGlnThrCys.....................GlnLeuL 26
         |:::      |||                        :::::::
      51 GGAGGKAGGTTTGTGTCGGACTGAACTCTTCCTCGTCCAGGTGCGTTTCT 100

      26 euLeuGluValAlaTrpProLeuPheIlePheLeuIleLeuIleSerVal 42
         :::::|||:::   |||||||||:::::::|||      |||:::   :::
     101 TTGTGGAGATCTTCTGGCCGTTGCTGCTCTTCAGCGGTCTGGTGTGGCTC 150

      43 ArgLeuSerTyrProProTyrGluGlnHisGluCys.............. 54
         |||   :::   |||   |||:::||||||||||
     151 AGGAAGGCCAACCCGCTGTACCAACAACATGAGTGTTAGABAACTCACAC 200

      54 ..................................................... 54

     201 ACTGGGCGACGTTTTCATCTGTCTTTTCTTTTTTCCATGTTAAAMAAACC 250

      55 ...................HisPheProAsnLysAla 60
                           ||||||||||||||||||
     251 CCTGCGTGCTTTCTCCAGGTCATTTCCCCAACAAAGCG 288

seq_name: gb_gss30:CNS01Y8B

seq_documentation_block:
LOCUS       CNS01Y8B      821 bp    DNA             GSS       12-MAY-2000
DEFINITION  Tetraodon nigroviridis genome survey sequence T7 end of clone
            217N20 of library G from Tetraodon nigroviridis, genomic survey
            sequence.
ACCESSION   AL172676
VERSION     AL172676.1  GI:7810733
KEYWORDS    GSS; genome survey sequence.
SOURCE      Tetraodon nigroviridis.
  ORGANISM  Tetraodon nigroviridis
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
            Eurypterygii; Ctenosquamata; Acanthomorpha; Euacanthomorpha;
            Holacanthopterygii; Acanthopterygii; Percomorpha;
            Tetraodontiformes; Tetraodontoidei; Tetraodontidae; Tetraodon.
REFERENCE   1  (bases 1 to 821)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Fizames,C., Fisher,C.,
            Bouneau,L., Billault,A., Quetier,F., Saurin,W., Bernot,A. and
            Weissenbach,J.
  TITLE     Charaterization and repeat analysis of the compact genome of the
            freshwater pufferfish Tetraodon nigroviridis
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 821)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Bouneau,L., Fisher,C.,
            Bernot,A., Fizames,C., Wincker,P., Brottier,P., Quetier,F.,
            Saurin,W. and Weissenbach,J.
  TITLE     Human gene number estimate provided by genome wide analysis using
            Tetraodon nigroviridis DNA sequence
  JOURNAL   Unpublished
REFERENCE   3  (bases 1 to 821)
  AUTHORS   Genoscope.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-APR-2000) to the EMBL/GenBank/DDBJ databases
COMMENT     This sequence is a single read and was generated as part of a large
            scale clone-end sequencing project of the Tetraodon nigroviridis
            genome. For more information, please take a look at
            http://www.genoscope.cns.fr/Tetraodon.
FEATURES             Location/Qualifiers
     source          1. .821
                     /organism="Tetraodon nigroviridis"
                     /db_xref="taxon:99883"
                     /clone="217N20"
                     /clone_lib="G"
                     /note="Genoscope sequence ID : C0AG217DG10LP1-end : T7"
BASE COUNT      173 a    205 c    239 g    200 t      4 others
ORIGIN


alignment_scores:
            Quality:   88.50             Length:     40
              Ratio:  2.950               Gaps:      1
 Percent Similarity:  75.000   Percent Identity: 42.500

alignment_block:
 US-09-526-193A-1_COPY_1_60 x CNS01Y8B   ..

 Align seg 1/1  to: CNS01Y8B  from: 1  to: 821

      17 PheArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLe 33
         |||      |||||:::  .:::|||:::::::|||:::   ||||||||
     666 TTCTGGCCTCGGCAGGTG...CGGCTGGTGGTGGAGTTGCTCTGGCCGCT 712

      33 uPheIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrG 50
         ||||::::|||||||||||||:::   ||||||   :::      |||::::
     713 CTTCCTCTTCCTGATCCTGGTGTGGGTGCGGACCACCAGCCAGCCCTTCC 762

      50 luGlnHisGluCysHisPhe 56
         :::::   :::|||   :::
     763 ACAAAGGCCAGTGTAAGTAT 782

seq_name: gb_est41:AW106575

seq_documentation_block:
LOCUS       AW106575      625 bp    mRNA            EST       20-OCT-1999
DEFINITION  um29h03.y1 Sugano mouse kidney mkia Mus musculus cDNA clone
            IMAGE:2235989 5' similar to TR:Q92473 Q92473 ABC-C TRANSPORTER. [1]
            ;, mRNA sequence.
ACCESSION   AW106575
VERSION     AW106575.1  GI:6077375
KEYWORDS    EST.
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 625)
  AUTHORS   Marra,M., Hillier,L., Kucaba,T., Martin,J., Beck,C., Wylie,T.,
            Underwood,K., Steptoe,M., Theising,B., Allen,M., Bowers,Y., Person
            ,B., Swaller,T., Gibbons,M., Pape,D., Harvey,N., Schurk,R., Ritter
            ,E., Kohn,S., Shin,T., Jackson,Y., Cardenas,M., McCann,R.,
            Waterston,R. and Wilson,R.
  TITLE     The WashU-NCI Mouse EST Project 1999
  JOURNAL   Unpublished (1999)
COMMENT     Contact: Marra M/WashU-NCI Mouse EST Project 1999
            Washington University School of Medicine
            4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108, USA
            Tel: 314 286 1800
            Fax: 314 286 1810
            Email: mouseest@watson.wustl.edu
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            MGI:1006201
            Seq primer: custom primer used
```

```
          High quality sequence stop: 394.
FEATURES             Location/Qualifiers
     source          1. .625
                     /organism="Mus musculus"
                     /strain="C57BL"
                     /db_xref="taxon:10090"
                     /clone="IMAGE:2235989"
                     /clone_lib="Sugano mouse kidney mkia"
                     /sex="female"
                     /dev_stage="adult"
                     /lab_host="DH10B"
                     /note="Organ: kidney; Vector: pME18S-FL3; Site_1: DraIII
                     (CACTGTGTG); Site_2: DraIII (CACCATGTG); 1st strand cDNA
                     was primed with an oligo(dT) primer
                     [ATGTGGCCTTTTTTTTTTTTTTTT]; double-stranded cDNA was
                     ligated to a  DraIII adaptor [TGTTGGCCTACTGG], digested
                     and cloned into distinct DraIII sites of the pME18S-FL3
                     vector (5' site CACTGTGTG, 3' site CACCATGTG). XhoI should
                     be used to isolate the cDNA insert.  Size selection was
                     performed to exclude fragments <1.5kb.  Library
                     constructed by Dr. Sumio Sugano (University of Tokyo
                     Institute of Medical Science).  Custom primers  for
                     sequencing: 5' end primer CTTCTGCTCTAAAAGCTGCG and 3' end
                     primer CGACCTGCAGCTCGAGCACA."
BASE COUNT      122 a    189 c    164 g    150 t
ORIGIN


alignment_scores:
            Quality:   85.50            Length:     67
              Ratio:  2.250              Gaps:      2
 Percent Similarity:  56.716   Percent Identity: 37.313

alignment_block:
 US-09-526-193A-1_COPY_1_60 x AW106575   ..

 Align seg 1/1  to: AW106575  from: 1  to: 625

       1 MetAlaCysTrpProGlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPh 17
         ||||||         ||||||   ||||||||||||||||||   |||::
     344 ATGGCAGTGCTGCGGCAGCTCACCCTCCTACTCTGGAAGAACTATACCCT 393

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         ::::::::|||::::::        :::|||   :::      ||||||:
     394 GAAGAAACGGAAGGTTCTAGTGACAGTCCTGTAGCTCTTCCTGCCCCTGC 443

      34 heIlePheLeuIleLeuIleSerValArgLeuSer..............  45
         :::::   :::||||||||||   :::|||||||:::
     444 TGTTATCTGTGATCCTGATTTGGCTTCGCTTGAAGATCCAGTCGGAGAAT 493

      46 ..................TyrProProTyrGluGlnHisGlu.CysHis 55
                           ||||||            :::||| ||||||
     494 GTGCCCAATGCCACTGTTTACCCGGACCAGTACATCCAGGAGCTGCCAC 542

seq_name: gb_gss31:CNS03SGV

seq_documentation_block:
LOCUS       CNS03SGV      823 bp    DNA             GSS       17-MAY-2000
DEFINITION  Tetraodon nigroviridis genome survey sequence T7 end of clone
            051L05 of library G from Tetraodon nigroviridis, genomic survey
            sequence.
ACCESSION   AL258520
VERSION     AL258520.1  GI:7979532
KEYWORDS    GSS; genome survey sequence.
SOURCE      Tetraodon nigroviridis.
  ORGANISM  Tetraodon nigroviridis
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
            Eurypterygii; Ctenosquamata; Acanthomorpha; Euacanthomorpha;
            Holacanthopterygii; Acanthopterygii; Percomorpha;
            Tetraodontiformes; Tetraodontoidei; Tetraodontidae; Tetraodon.
REFERENCE   1  (bases 1 to 823)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Fizames,C., Fisher,C.,
            Bouneau,L., Billault,A., Quetier,F., Saurin,W., Bernot,A. and
            Weissenbach,J.
  TITLE     Charaterization and repeat analysis of the compact genome of the
            freshwater pufferfish Tetraodon nigroviridis
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 823)
  AUTHORS   Roest-Crollius,H., Jaillon,O., Dasilva,C., Bouneau,L., Fisher,C.,
            Bernot,A., Fizames,C., Wincker,P., Brottier,P., Quetier,F.,
            Saurin,W. and Weissenbach,J.
  TITLE     Human gene number estimate provided by genome wide analysis using
            Tetraodon nigroviridis DNA sequence
  JOURNAL   Unpublished
REFERENCE   3  (bases 1 to 823)
  AUTHORS   Genoscope.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-APR-2000) to the EMBL/GenBank/DDBJ databases
COMMENT     This sequence is a single read and was generated as part of a large
            scale clone-end sequencing project of the Tetraodon nigroviridis
            genome. For more information, please take a look at
            http://www.genoscope.cns.fr/Tetraodon.
FEATURES             Location/Qualifiers
     source          1. .823
                     /organism="Tetraodon nigroviridis"
                     /db_xref="taxon:99883"
                     /clone="051L05"
                     /clone_lib="G"
                     /note="Genoscope sequence ID : C0BG051CF03LP1-end : T7"
BASE COUNT      193 a    205 c    173 g    245 t      7 others
ORIGIN


alignment_scores:
            Quality:   84.00            Length:     35
              Ratio:  3.360              Gaps:      0
 Percent Similarity:  71.429   Percent Identity: 42.857

alignment_block:
 US-09-526-193A-1_COPY_1_60 x CNS03SGV   ..

 Align seg 1/1  to: CNS03SGV  from: 1  to: 823

      26 LeuLeuGluValAlaTrpProLeuPheIlePheLeuIleLeuIleSerVa 42
         |||:::|||:::   ||||||::::::::|||:::   |||:::   ::
      12 CTCATGGAGATCATGTGGCCTGTCCTGCTGTTTGTGGGCCTGGTGTGGCT 61

      42 lArgLeuSerTyrProProTyrGluGlnHisGluCysHisPheProAsnL 59
         :|||         |||   |||:::||||||||||||:::   |||
      62 GCGGAGGGTGAACCCTCTGTACCGCCAACACGAATGTGAGGAACCAGCAC 111

      59 ysAla 60
           |||
     112 CGGCG 116

seq_name: gb_gss27:B29539

seq_documentation_block:
LOCUS       B29539         554 bp    DNA             GSS       13-OCT-1997
DEFINITION  T10K17TFB TAMU Arabidopsis thaliana genomic clone T10K17, DNA
            sequence.
ACCESSION   B29539
VERSION     B29539.1  GI:2515505
KEYWORDS    GSS.
SOURCE      thale cress.
  ORGANISM  Arabidopsis thaliana
            Eukaryota; Viridiplantae; Embryophyta; Tracheophyta; Spermatophyta;
            Magnoliophyta; eudicotyledons; core eudicots; Rosidae; eurosids II;
            Brassicales; Brassicaceae; Arabidopsis.
REFERENCE   1  (bases 1 to 554)
  AUTHORS   Rounsley,S.D., Kelley,J.M., Field,C.E., Craven,M.B., Adams,M.D. and
            Venter,J.C.
  TITLE     Use of a BAC End Sequence Database To Identify Minimal Overlaps for
            Arabidopsis Genomic Sequencing
  JOURNAL   Unpublished (1997)
```

```
COMMENT     Other_GSSs: T10K17TRB
            Contact: Steve Rounsley
            Department of Eukaryotic Genomics
            The Institute for Genomic Research
            9712 Medical Center Dr., Rockville, MD 20850, USA
            Tel: 301 838 0200
            Fax: 301 838 0208
            Email: rounsley@tigr.org
            Seq primer: M13-21
            Class: BAC ends
            High quality sequence stop: 554.
FEATURES              Location/Qualifiers
     source           1. .554
                      /organism="Arabidopsis thaliana"
                      /strain="Columbia"
                      /db_xref="taxon:3702"
                      /clone="T10K17"
                      /clone_lib="TAMU"
                      /sex="hermaphrodite"
                      /note="Vector: BeloBACII; Site_1: HindIII; Site_2: HindIII
                      ; Produced by Rod Wing"
BASE COUNT      166 a    108 c    133 g    145 t      2 others
ORIGIN


alignment_scores:
            Quality:   78.00             Length:     38
              Ratio:  3.120               Gaps:      1
 Percent Similarity:  65.789   Percent Identity: 44.737

alignment_block:
 US-09-526-193A-1_COPY_1_60 x B29539/rev   ..

 Align seg 1/1  to reverse of: B29539  from: 1  to: 554

      20 ArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIle.. 35
         |||:::||||||:::||||||         |||   |||   |||:::
     231 AGAAAGACTTGCGAACTTCTGTACCCTCAAGCCATTCCCCGCTTCCTACA 182

      36 ....PheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGluG 51
             ||||||||||:::   :::|||   ||||||      :::|||
     181 GTGCCACTTGATATTGGTTCATCTTCGGCAATCATACAATCAGTTTGAGG 132

      51 lnHisGluCysHis 55
         |||:::::::|||
     131 TTCATCAGGCACAC 118

seq_name: gb_est17:AI220973

seq_documentation_block:
LOCUS       AI220973      478 bp    mRNA            EST       29-NOV-1998
DEFINITION  qg04a04.x1 Soares_placenta_8to9weeks_2NbHP8to9W Homo sapiens cDNA
            clone IMAGE:1758510 3', mRNA sequence.
ACCESSION   AI220973
VERSION     AI220973.1  GI:3803176
KEYWORDS    EST.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 478)
  AUTHORS   NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap.
  TITLE     National Cancer Institute, Cancer Genome Anatomy Project (CGAP),
            Tumor Gene Index
  JOURNAL   Unpublished (1997)
COMMENT     Contact: Robert Strausberg, Ph.D.
            Tel: (301) 496-1550
            Email: Robert_Strausberg@nih.gov
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            Insert Length: 993   Std Error: 0.00
            Seq primer: -40UP from Gibco
            High quality sequence stop: 463.
FEATURES              Location/Qualifiers
     source           1. .478
                      /organism="Homo sapiens"
                      /db_xref="taxon:9606"
                      /clone="IMAGE:1758510"
                      /clone_lib="Soares_placenta_8to9weeks_2NbHP8to9W"
                      /dev_stage="two placentae: one from 8 weeks and another
                      from 9 weeks post conception"
                      /lab_host="DH10B (ampicillin resistant)"
                      /note="Organ: placenta; Vector: pT7T3D (Pharmacia) with a
                      modified polylinker; Site_1: Not I; Site_2: Eco RI; 1st
                      strand cDNA was primed with a Not I - oligo(dT) primer [5'
                      TGTTACCAATCTGAAGTGGGAGCGGCCGCGATTTTTTTTTTTTTTTTT 3'],
                      double-stranded cDNA was size selected, ligated to Eco RI
                      adapters (Pharmacia), digested with Not I and cloned into
                      the Not I and Eco RI sites of a modified pT7T3 vector
                      (Pharmacia). Library constructed by Bento Soares and
                      M.Fatima Bonaldo."
BASE COUNT      128 a    110 c    114 g    126 t
ORIGIN


alignment_scores:
            Quality:   76.00             Length:     50
              Ratio:  2.533               Gaps:      1
 Percent Similarity:  60.000   Percent Identity: 36.000

alignment_block:
 US-09-526-193A-1_COPY_1_60 x AI220973   ..

 Align seg 1/1  to: AI220973  from: 1  to: 478

       4 TrpProGlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgAr 20
         |||   |||   |||   ||||||   ||||||      ::::::   ||
     263 TGGAGACAGACCAGAACACTTCTACTGAAGAATTACTTAATTAAATGCAG 312

      20 gGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheL 37
         |         :::   :::   |||:::   :::||||||||||:::|||:
     313 AACCAAAAAGAGTAGTGTTCAGGAAATTCTTTTTCCACTATTTTTTTTTT 362

      37 euIleLeuIleSerValArgLeuSerTyrPro......ProTyrGluGln 51
         ::   ||||||   :::   :::   :::|||         ||||||:::
     363 TTTGGTTAATATTAATTAGCATGATGCATCCAAATAAGACATATGAAGAA 412

seq_name: gb_est16:AI149299

seq_documentation_block:
LOCUS       AI149299      510 bp    mRNA            EST       28-OCT-1998
DEFINITION  qc72c12.x1 Soares_placenta_8to9weeks_2NbHP8to9W Homo sapiens cDNA
            clone IMAGE:1715158 3', mRNA sequence.
ACCESSION   AI149299
VERSION     AI149299.1  GI:3677768
KEYWORDS    EST.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 510)
  AUTHORS   NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap.
  TITLE     National Cancer Institute, Cancer Genome Anatomy Project (CGAP),
            Tumor Gene Index
  JOURNAL   Unpublished (1997)
COMMENT     Contact: Robert Strausberg, Ph.D.
            Tel: (301) 496-1550
            Email: Robert_Strausberg@nih.gov
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            Insert Length: 995   Std Error: 0.00
            Seq primer: -40m13 fwd. ET from Amersham
            High quality sequence stop: 437.
FEATURES              Location/Qualifiers
     source           1. .510
                      /organism="Homo sapiens"
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                     /db_xref="taxon:9606"
                     /clone="IMAGE:1715158"
                     /clone_lib="Soares_placenta_8to9weeks_2NbHP8to9W"
                     /dev_stage="two placentae: one from 8 weeks and another
                     from 9 weeks post conception"
                     /lab_host="DH10B (ampicillin resistant)"
                     /note="Organ: placenta; Vector: pT7T3D (Pharmacia) with a
                     modified polylinker; Site_1: Not I; Site_2: Eco RI; 1st
                     strand cDNA was primed with a Not I - oligo(dT) primer [5'
                     TGTTACCAATCTGAAGTGGGAGCGGCCGCGATTTTTTTTTTTTTTTTT 3'],
                     double-stranded cDNA was size selected, ligated to Eco RI
                     adapters (Pharmacia), digested with Not I and cloned into
                     the Not I and Eco RI sites of a modified pT7T3 vector
                     (Pharmacia). Library constructed by Bento Soares and
                     M.Fatima Bonaldo."
BASE COUNT      142 a    117 c    118 g    132 t      1 others
ORIGIN


alignment_scores:
            Quality:   76.00             Length:     50
              Ratio:  2.533               Gaps:      1
 Percent Similarity:  60.000   Percent Identity: 36.000

alignment_block:
 US-09-526-193A-1_COPY_1_60 x AI149299  ..

 Align seg 1/1  to: AI149299  from: 1  to: 510

       4 TrpProGlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgAr 20
         |||   |||   |||   ||||||      ::::::   ||
     263 TGGAGACAGACCAGAACACTTCTACTGAAGAATTACTTAATTAAATGCAG 312

      20 gGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheL 37
         |        :::   :::   |||:::   :::||||||||||:::|||:
     313 AACCAAAAAGAGTAGTGTTCAGGAAATTCTTTTTCCACTATTTTTTTTTT 362

      37 euIleLeuIleSerValArgLeuSerTyrPro......ProTyrGluGln 51
         ::   ||||||   :::   :::   :::|||         ||||||:::
     363 TTTGGTTAATATTAATTAGCATGATGCATCCAAATAAGAAATATGAAGAA 412

seq_name: gb_gss29:CNS008DW

seq_documentation_block:
LOCUS       CNS008DW      961 bp    DNA             GSS       03-JUN-1999
DEFINITION  Drosophila melanogaster genome survey sequence T7 end of BAC #
            BACR17C05 of RPCI-98 library from Drosophila melanogaster (fruit
            fly), genomic survey sequence.
ACCESSION   AL052459
VERSION     AL052459.1  GI:4933604
KEYWORDS    GSS.
SOURCE      fruit fly.
  ORGANISM  Drosophila melanogaster
            Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
            Pterygota; Neoptera; Endopterygota; Diptera; Brachycera;
            Muscomorpha; Ephydroidea; Drosophilidae; Drosophila.
REFERENCE   1  (bases 1 to 961)
  AUTHORS   Genoscope.
  TITLE     Direct Submission
  JOURNAL   Submitted (02-JUN-1999) Genoscope - Centre National de Sequencage :
            BP 191 91006 EVRY cedex - FRANCE (E-mail : seqref@genoscope.cns.fr
            - Web : www.genoscope.cns.fr)
COMMENT     Determination of this BAC-end sequence was carried out as part of a
            collaboration with the Berkeley Drosophila Genome Project (BDGP).
            The BDGP is constructing a physical map of the Drosophila
            melanogaster genome using these BACs. For further information
            please see  http://www.fruitfly.org The BDGP Drosophila
            melanogaster BAC library was prepared by Kazutoyo Osoegawa and
            Aaron Mammoser in Pieter de Jong's laboratory in the Department of
            Cancer Genetics at the Roswell Park Cancer Institute in Buffalo,
            NY. The library is named RPCI-98 and was constructed by partial
            EcoRI digestion of Drosophila DNA provided by the BDGP from the
            isogenic strain y2; cn bw sp, the same strain used for the BDGP's
            P1 and EST libraries. A more detailed description of the library
            and how to order individual BAC clones, the entire library, or
            filters for hybridization from the BACPAC Resource Center can be
            found at http://bacpac.med.buffalo.edu/drosophila_bac.htm.
FEATURES             Location/Qualifiers
     source          1. .961
                     /organism="Drosophila melanogaster"
                     /db_xref="taxon:7227"
                     /clone_lib="RPCI-98"
                     /clone="BACR17C05"
                     /note="end : T7"
BASE COUNT      317 a    217 c    167 g    213 t     47 others
ORIGIN


alignment_scores:
            Quality:   75.50             Length:     64
              Ratio:  2.288               Gaps:      4
 Percent Similarity:  51.562   Percent Identity: 34.375

alignment_block:
 US-09-526-193A-1_COPY_1_60 x CNS008DW/rev  ..

 Align seg 1/1  to reverse of: CNS008DW  from: 1  to: 961

       3 CysTrpProGlnLeuArgLeuLeuLeuTrpLysAsn..............  14
         |||   |||   :::   |||:::||||||:::
     693 TGCGCCCCGTTCTTTGCCCTTTTTCTGTGGCGCCCAAAAAAATGGGCTGT 644

      15 ..................LeuThrPheArgArgArgGlnThrCysGlnL  25
                             :::   ||||||   |||:::
     643 GGCTTACGACCAGGTCTGATTCGGATTTCGCCTCCGACACCGA.......  601

      25 euLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleLeuIleSer  41
           ||||||||||||||||||   |||:::::|||   :::|||::::::
     600 ..CTCCTTGAGGTGGCGTGGCAGCTCTGGCTCTTTCGCCTCCTTCTGGCC 553

      42 ValArgLeuSerTyrProProTyrGluGlnHisGluCysHis 55
                 |||||||||   :::            ||||||
     552 .........TCTTATCCAGCGCAC............TGCCAT 532

seq_name: gb_est87:BF442774

seq_documentation_block:
LOCUS       BF442774      427 bp    mRNA            EST       01-DEC-2000
DEFINITION  260029 MARC 2PIG Sus scrofa cDNA 5', mRNA sequence.
ACCESSION   BF442774
VERSION     BF442774.1  GI:11502866
KEYWORDS    EST.
SOURCE      pig.
  ORGANISM  Sus scrofa
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
REFERENCE   1  (bases 1 to 427)
  AUTHORS   Fahrenkrug,S.C., Freking,B.A., Rohrer,G.A., Smith,T.P.L., Casas,E.,
            Stone,R.T., Heaton,M.P., Grosse,W.M., Bennett,G.A., Laegreid,W.W.
            and Keele,J.W.
  TITLE     Design and use of two pooled tissue normalized cDNA libraries for
            EST discovery in swine
  JOURNAL   Unpublished (2000)
COMMENT     Contact: Smith TPL
            USDA, ARS, US Meat Animal Research Center
            PO Box 166, Clay Center, NE 68933-0166, USA
            Tel: 402 762 4366
            Fax: 402 762 4390
            Email: smith@email.marc.usda.gov
            Single pass sequencing. Bases called and alt_trimmed with phred
            v0.980904.e. Vector identified by cross_match with the -minscore 18
            and -minmatch 12 options.
            PCR PRimers
            FORWARD: AGGAAACAGCTATGACCAT
            BACKWARD: GTTTTCCCAGTCACGACG
            Plate: 91  row: M  column: 9
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           Seq primer: ATTTAGGTGACACTATAG.
FEATURES             Location/Qualifiers
     source          1. .427
                     /organism="Sus scrofa"
                     /db_xref="taxon:9823"
                     /clone_lib="MARC 2PIG"
                     /tissue_type="pooled"
                     /lab_host="DH10B"
                     /note="Vector: pCMV SPORT6; Site_1: XbaI; Site_2: XhoI;
                     Library made from pooled tissue from testis, ovary,
                     endometrium, hypothalamus, pituitary, and placenta."
BASE COUNT       96 a     89 c    122 g    120 t
ORIGIN


alignment_scores:
            Quality:   75.00             Length:     38
              Ratio:  2.679               Gaps:       0
 Percent Similarity:  73.684   Percent Identity: 42.105

alignment_block:
 US-09-526-193A-1_COPY_1_60 x BF442774   ..

 Align seg 1/1  to: BF442774  from: 1  to: 427

       6 GlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGlnTh 22
         |||:::   :::||||||||||||||||:::|||::::::|||||||||
     227 CAATTTGCAGTGCTCCTCTGGAAAAATTTTACCTTAAAGAGGAGGCAGTT 276

      22 rCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleL 39
          :::|||:::||||||:::         |||   :::   ::::::|
     277 CTTTAATTTAATGTTGGAAATCCTAGCAGCATTGGTGTTTCCCGTGATGC 326

      39 euIleSerValArg 43
         ||:::      |||
     327 TTTTGCTGTTCCGT 340
```

OM of: US-09-526-193A-1_COPY_1_60 to: N_Geneseq_0401:* out_format : pfs

Date: Jun 2, 2001 8:13 PM

About: Results were produced by the GenCore software, version 4.5,
Copyright (c) 1993-2000 Compugen Ltd.

Command line parameters:
-MODEL=frame+_p2n.model -DEV=xlp
-Q=/cgn2_1/USPTO_spool/US09526193/runat_01062001_202006_15762/app_query.fasta_1.128
-DB=N_Geneseq_0401 -QFMT=fastap -SUFFIX=rng -GAPOP=12.000
-GAPEXT=4.000 -MINMATCH=0.100 -LOOPCL=0.000 -LOOPEXT=0.000
-QGAPOP=4.500 -QGAPEXT=0.050 -XGAPOP=10.000 -XGAPEXT=0.500
-FGAPOP=6.000 -FGAPEXT=7.000 -YGAPOP=10.000 -YGAPEXT=0.500
-DELOP=6.000 -DELEXT=7.000 -START=1 -MATRIX=blosum62
-TRANS=human40.cdi -LIST=45 -DOCALIGN=200 -THR_SCORE=pct
-THR_MAX=100 -THR_MIN=0 -ALIGN=15 -MODE=LOCAL -OUTFMT=pfs
-NORM=ext -MINLEN=0 -MAXLEN=2000000000
-USER=US09526193_@CGN1_1_174 -NCPU=6 -ICPU=3 -LONGLOG -NO_XLPXY
-WAIT -THREADS=1

Search information block:
Query: US-09-526-193A-1_COPY_1_60
Query length: 60
Database: N_Geneseq_0401:*
Database sequences: 678276
Database length: 291890651
Search time (sec): 127.230000

score_list:

Sequence	Strd	Orig	ZScore	EScore	Len	! Documentation ..
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69388	+	334.00	764.14	1.3e-34	7857	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69387	+	334.00	764.14	1.3e-34	7861	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69120	+	334.00	764.14	1.3e-34	7864	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69385	+	334.00	764.14	1.3e-34	7864	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69386	+	334.00	764.14	1.3e-34	7864	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69389	+	334.00	764.14	1.3e-34	7864	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C75311	+	230.00	540.36	3.7e-22	534	! Hu
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:Z94734	+	220.00	489.40	2.5e-19	6880	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C88565	+	180.00	416.12	3.1e-15	720	! Hu
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:Z94746	+	180.00	391.85	6.9e-14	7323	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA1998.DAT:V33392	+	180.00	391.21	7.5e-14	7784	! A
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69133	+	176.50	387.94	1.1e-13	4736	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69132	+	131.00	269.35	4.6e-07	10545	!
/SIDS6/gcgdata/geneseq/geneseqn/NA1998.DAT:V16345	+	86.00	165.37	0.2844	6525	! c
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:Z94761	+	84.00	160.58	0.5257	6491	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA1997.DAT:V74631	-	76.50	143.42	4.75	5897	! S
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C55023	-	70.00	151.48	1.69	606	! Ar
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C52472	-	70.00	151.14	1.76	626	! Ar
/SIDS6/gcgdata/geneseq/geneseqn/NA1999.DAT:X60142	+	67.50	131.77	21.16	2235	! S
/SIDS6/gcgdata/geneseq/geneseqn/NA1998.DAT:V52185	+	67.50	110.79	311.86	16593	!
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C93314	+	65.00	136.23	11.94	818	! Hu
/SIDS6/gcgdata/geneseq/geneseqn/NA1998.DAT:V62392	-	65.00	107.64	466.87	12565	!
/SIDS6/gcgdata/geneseq/geneseqn/NA1999.DAT:X75925	-	65.00	107.64	466.87	12565	!
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C63769	-	65.00	107.64	466.87	12565	!
/SIDS6/gcgdata/geneseq/geneseqn/NA2001.DAT:C91435	-	65.00	107.64	466.87	12565	!
/SIDS6/gcgdata/geneseq/geneseqn/NA1999.DAT:V87050	-	63.50	139.01	8.36	443	! ES
/SIDS6/gcgdata/geneseq/geneseqn/NA1992.DAT:Q33025	+	63.50	136.54	11.47	561	! Ex
/SIDS6/gcgdata/geneseq/geneseqn/NA1998.DAT:V40501	-	63.50	133.95	16.00	719	! Hu
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A47427	-	63.50	123.88	58.17	1881	! S
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A89688	+	63.00	138.26	9.20	424	! Mo
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A89686	+	63.00	138.24	9.23	425	! Mo
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A89689	+	63.00	137.34	10.36	463	! Mo
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A89687	+	63.00	136.75	11.17	490	! Mo
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A89685	+	63.00	136.58	11.42	498	! Mo
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:Z46508	-	62.50	88.18	5.7e+03	45265	!
/SIDS6/gcgdata/geneseq/geneseqn/NA1997.DAT:T85826	+	62.00	122.35	70.82	1539	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:F20878	-	62.00	106.02	575.03	7328	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:F20887	-	62.00	106.02	575.03	7328	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A34752	-	62.00	106.02	575.03	7328	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A34756	-	62.00	106.02	575.03	7328	! H
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A34765	-	62.00	106.02	575.03	7328	
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:F21451	-	62.00	86.28	7.2e+03	48333	
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:F21435	-	62.00	76.98	2.4e+04	117609	
/SIDS6/gcgdata/geneseq/geneseqn/NA1991.DAT:Q11140	-	61.50	117.36	134.27	2208	
/SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:A50020	+	61.50	114.49	194.04	2905	

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69388

seq_documentation_block:
ID C69388 standard; cDNA; 7857 BP.
XX
AC C69388;
XX
DT 29-JAN-2001 (first entry)
XX
DE Human ABC1 cholesterol transporter FHA-3 mutant cDNA (delta 5752-5757).
XX
KW Human ABC1 cholesterol transporter; chromosome 9q31;
KW ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW cardiovascular disease; coronary artery disease; coronary restenosis;
KW cerebrovascular disease; peripheral vascular disease;
KW Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
KW X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW prognosis; prophylaxis; drug screening; transgenic animal; mutant; ss.
XX
OS Homo sapiens.
XX
PN WO200055318-A2.
XX
PD 21-SEP-2000.
XX
PF 15-MAR-2000; 2000WO-IB00532.
XX
PR 15-MAR-1999; 99US-0124702.
PR 08-JUN-1999; 99US-0138048.
PR 17-JUN-1999; 99US-0139600.
PR 01-SEP-1999; 99US-0151977.
XX
PA (UYBR-) UNIV BRITISH COLUMBIA.
PA (XENO-) XENON BIORESEARCH INC.
XX
PI Hayden MR, Wilson AR, Pimstone SN;
XX
DR WPI; 2000-587528/55.
DR P-PSDB; B38107.
XX
PT New ABC1 polypeptide is useful for treating diseases associated with
PT ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT disease and cancer -
XX
PS Examples; Page -; 229pp; English.
XX
CC The invention relates to the human ABC1 cholesterol transporter protein
CC (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC a member of the ATP-binding cassette (ABC transporter) superfamily of
CC proteins, and plays a crucial role in cholesterol transport, particularly
CC intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC located on chromosome 9q31, and mutations in this gene are associated
CC with two genetic HDL (high density lipoprotein) deficiency disorders,
CC Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC are distinguishable in that TD is an autosomal recessive disorder, while
CC FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC cholesterol") in the blood correlate with a high risk of cardiovascular
CC disease, particularly coronary artery disease, but also cerebrovascular
CC disease, coronary restenosis, and peripheral vascular disease.
CC Conversely, a high level of HDL has protective effects against
CC cardiovascular disease. The invention provides genetic constructs and
CC transgenic cells and non-human animals comprising human ABC1 nucleic
CC acids, and methods of gene therapy for the treatment or prevention of
CC cardiovascular disease comprising the administration of an expression
CC vector encoding ABC1 or an active fragment thereof. The invention also

```
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1. The
CC   present sequence represents cDNA encoding a mutant human ABC1 cholesterol
CC   transporter associated with an altered cholesterol level and therefore an
CC   altered risk of cardiovascular disease.
CC   Note: The present sequence is not shown in the specification, but is
CC   derived from the native human ABC1 cDNA shown on pages 157-160.
XX
SQ   Sequence 7857 BP; 2011 A; 1860 C; 2008 G; 1977 T; 1 other;


alignment_scores:
            Quality:  334.00              Length:     60
              Ratio:  5.567                Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-526-193A-1_COPY_1_60 x C69388   ..

 Align seg 1/1  to: C69388  from: 1  to: 7857

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         ||||||||||||||||||||||||||||||||||||||||||||||||||
      75 ATGGCTTGTTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 124

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     125 CAGAAGAAGACAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTAT 174

      34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     175 TTATCTTCCTGATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAA 224

      51 GlnHisGluCysHisPheProAsnLysAla 60
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seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69387

seq_documentation_block:
ID   C69387 standard; cDNA; 7861 BP.
XX
AC   C69387;
XX
DT   29-JAN-2001  (first entry)
XX
DE   Human ABC1 cholesterol transporter FHA-1 mutant cDNA (delta 2151-2153).
XX
KW   Human ABC1 cholesterol transporter; chromosome 9q31;
KW   ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW   Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW   cardiovascular disease; coronary artery disease; coronary restenosis;
KW   cerebrovascular disease; peripheral vascular disease;
KW   Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
KW   X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW   prognosis; prophylaxis; drug screening; transgenic animal; mutant; ss.
XX
OS   Homo sapiens.
XX
PN   WO200055318-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-IB00532.
XX
PR   15-MAR-1999;   99US-0124702.
PR   08-JUN-1999;   99US-0138048.
PR   17-JUN-1999;   99US-0139600.
PR   01-SEP-1999;   99US-0151977.
XX
PA   (UYBR-) UNIV BRITISH COLUMBIA.
PA   (XENO-) XENON BIORESEARCH INC.
XX
PI   Hayden MR,  Wilson AR,  Pimstone SN;
XX
DR   WPI; 2000-587528/55.
DR   P-PSDB; B38106.
XX
PT   New ABC1 polypeptide is useful for treating diseases associated with
PT   ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT   disease and cancer -
XX
PS   Examples; Page -; 229pp; English.
XX
CC   The invention relates to the human ABC1 cholesterol transporter protein
CC   (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC   a member of the ATP-binding cassette (ABC transporter) superfamily of
CC   proteins, and plays a crucial role in cholesterol transport, particularly
CC   intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC   involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC   located on chromosome 9q31, and mutations in this gene are associated
CC   with two genetic HDL (high density lipoprotein) deficiency disorders,
CC   Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC   are distinguishable in that TD is an autosomal recessive disorder, while
CC   FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC   cholesterol") in the blood correlate with a high risk of cardiovascular
CC   disease, particularly coronary artery disease, but also cerebrovascular
CC   disease, coronary restenosis, and peripheral vascular disease.
CC   Conversely, a high level of HDL has protective effects against
CC   cardiovascular disease. The invention provides genetic constructs and
CC   transgenic cells and non-human animals comprising human ABC1 nucleic
CC   acids, and methods of gene therapy for the treatment or prevention of
CC   cardiovascular disease comprising the administration of an expression
CC   vector encoding ABC1 or an active fragment thereof. The invention also
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1. The
CC   present sequence represents cDNA encoding a mutant human ABC1 cholesterol
CC   transporter associated with an altered cholesterol level and therefore an
CC   altered risk of cardiovascular disease.
CC   Note: The present sequence is not shown in the specification, but is
CC   derived from the native human ABC1 cDNA shown on pages 157-160.
XX
SQ   Sequence 7861 BP; 2014 A; 1859 C; 2011 G; 1976 T; 1 other;


alignment_scores:
            Quality:  334.00              Length:     60
              Ratio:  5.567                Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
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 Align seg 1/1  to: C69387  from: 1  to: 7861
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     75 ATGGCTTGTTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 124

     17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    125 CAGAAGAAGACAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTAT 174

     34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    175 TTATCTTCCTGATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAA 224

     51 GlnHisGluCysHisPheProAsnLysAla 60
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    225 CAACATGAATGCCATTTTCCAAATAAAGCC 254

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69120

seq_documentation_block:
ID   C69120 standard; cDNA; 7864 BP.
XX
AC   C69120;
XX
DT   29-JAN-2001  (first entry)
XX
DE   Human ABC1 cholesterol transporter cDNA.
XX
KW   Human ABC1 cholesterol transporter; chromosome 9q31;
KW   ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW   Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW   cardiovascular disease; coronary artery disease; coronary restenosis;
KW   cerebrovascular disease; peripheral vascular disease;
KW   Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
KW   X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW   prognosis; prophylaxis; drug screening; transgenic animal; ss.
XX
OS   Homo sapiens.
XX
PN   WO200055318-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-IB00532.
XX
PR   15-MAR-1999;   99US-0124702.
PR   08-JUN-1999;   99US-0138048.
PR   17-JUN-1999;   99US-0139600.
PR   01-SEP-1999;   99US-0151977.
XX
PA   (UYBR-) UNIV BRITISH COLUMBIA.
PA   (XENO-) XENON BIORESEARCH INC.
XX
PI   Hayden MR,  Wilson AR,  Pimstone SN;
XX
DR   WPI; 2000-587528/55.
DR   P-PSDB; B38082.
XX
PT   New ABC1 polypeptide is useful for treating diseases associated with
PT   ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT   disease and cancer -
XX
PS   Claim 13; Page 157-160; 229pp; English.
XX
CC   The invention relates to the human ABC1 cholesterol transporter protein
CC   (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC   a member of the ATP-binding cassette (ABC transporter) superfamily of
CC   proteins, and plays a crucial role in cholesterol transport, particularly
CC   intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC   involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC   located on chromosome 9q31, and mutations in this gene are associated
CC   with two genetic HDL (high density lipoprotein) deficiency disorders,
CC   Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC   are distinguishable in that TD is an autosomal recessive disorder, while
CC   FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC   cholesterol") in the blood correlate with a high risk of cardiovascular
CC   disease, particularly coronary artery disease, but also cerebrovascular
CC   disease, coronary restenosis, and peripheral vascular disease.
CC   Conversely, a high level of HDL has protective effects against
CC   cardiovascular disease. The invention provides genetic constructs and
CC   transgenic cells and non-human animals comprising human ABC1 nucleic
CC   acids, and methods of gene therapy for the treatment or prevention of
CC   cardiovascular disease comprising the administration of an expression
CC   vector encoding ABC1 or an active fragment thereof. The invention also
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1. The
CC   present sequence represents cDNA encoding the human ABC1 cholesterol
CC   transporter.
XX
SQ   Sequence 7864 BP; 2014 A; 1860 C; 2011 G; 1978 T; 1 other;


alignment_scores:
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              Ratio:  5.567                Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
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     75 ATGGCTTGTTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 124

     17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    125 CAGAAGAAGACAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTAT 174

     34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    175 TTATCTTCCTGATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAA 224

     51 GlnHisGluCysHisPheProAsnLysAla 60
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    225 CAACATGAATGCCATTTTCCAAATAAAGCC 254

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69385

seq_documentation_block:
ID   C69385 standard; cDNA; 7864 BP.
XX
AC   C69385;
XX
DT   29-JAN-2001  (first entry)
XX
DE   Human ABC1 cholesterol transporter TD-1 mutant cDNA (T4503C).
XX
KW   Human ABC1 cholesterol transporter; chromosome 9q31;
KW   ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW   Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW   cardiovascular disease; coronary artery disease; coronary restenosis;
KW   cerebrovascular disease; peripheral vascular disease;
KW   Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
```

```
KW   X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW   prognosis; prophylaxis; drug screening; transgenic animal; mutant; ss.
XX
OS   Homo sapiens.
XX
PN   WO200055318-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-IB00532.
XX
PR   15-MAR-1999;   99US-0124702.
PR   08-JUN-1999;   99US-0138048.
PR   17-JUN-1999;   99US-0139600.
PR   01-SEP-1999;   99US-0151977.
XX
PA   (UYBR-) UNIV BRITISH COLUMBIA.
PA   (XENO-) XENON BIORESEARCH INC.
XX
PI   Hayden MR,  Wilson AR,  Pimstone SN;
XX
DR   WPI; 2000-587528/55.
DR   P-PSDB; B38104.
XX
PT   New ABC1 polypeptide is useful for treating diseases associated with
PT   ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT   disease and cancer -
XX
PS   Examples; Page -; 229pp; English.
XX
CC   The invention relates to the human ABC1 cholesterol transporter protein
CC   (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC   a member of the ATP-binding cassette (ABC transporter) superfamily of
CC   proteins, and plays a crucial role in cholesterol transport, particularly
CC   intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC   involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC   located on chromosome 9q31, and mutations in this gene are associated
CC   with two genetic HDL (high density lipoprotein) deficiency disorders,
CC   Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC   are distinguishable in that TD is an autosomal recessive disorder, while
CC   FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC   cholesterol") in the blood correlate with a high risk of cardiovascular
CC   disease, particularly coronary artery disease, but also cerebrovascular
CC   disease, coronary restenosis, and peripheral vascular disease.
CC   Conversely, a high level of HDL has protective effects against
CC   cardiovascular disease. The invention provides genetic constructs and
CC   transgenic cells and non-human animals comprising human ABC1 nucleic
CC   acids, and methods of gene therapy for the treatment or prevention of
CC   cardiovascular disease comprising the administration of an expression
CC   vector encoding ABC1 or an active fragment thereof. The invention also
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1. The
CC   present sequence represents cDNA encoding a mutant human ABC1 cholesterol
CC   transporter associated with an altered cholesterol level and therefore an
CC   altered risk of cardiovascular disease.
CC   Note: The present sequence is not shown in the specification, but is
CC   derived from the native human ABC1 cDNA shown on pages 157-160.
XX
SQ   Sequence 7864 BP; 2014 A; 1861 C; 2011 G; 1977 T; 1 other;

alignment_scores:
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 Percent Similarity: 100.000   Percent Identity: 100.000

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      75 ATGGCTTGTTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 124

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     125 CAGAAGAAGACAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTAT 174

      34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     175 TTATCTTCCTGATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAA 224

      51 GlnHisGluCysHisPheProAsnLysAla 60
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     225 CAACATGAATGCCATTTTCCAAATAAAGCC 254

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69386

seq_documentation_block:
ID   C69386 standard; cDNA; 7864 BP.
XX
AC   C69386;
XX
DT   29-JAN-2001  (first entry)
XX
DE   Human ABC1 cholesterol transporter TD-2 mutant cDNA (A1864G).
XX
KW   Human ABC1 cholesterol transporter; chromosome 9q31;
KW   ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW   Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW   cardiovascular disease; coronary artery disease; coronary restenosis;
KW   cerebrovascular disease; peripheral vascular disease;
KW   Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
KW   X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW   prognosis; prophylaxis; drug screening; transgenic animal; mutant; ss.
XX
OS   Homo sapiens.
XX
PN   WO200055318-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-IB00532.
XX
PR   15-MAR-1999;   99US-0124702.
PR   08-JUN-1999;   99US-0138048.
PR   17-JUN-1999;   99US-0139600.
PR   01-SEP-1999;   99US-0151977.
XX
PA   (UYBR-) UNIV BRITISH COLUMBIA.
PA   (XENO-) XENON BIORESEARCH INC.
XX
PI   Hayden MR,  Wilson AR,  Pimstone SN;
XX
DR   WPI; 2000-587528/55.
DR   P-PSDB; B38105.
XX
PT   New ABC1 polypeptide is useful for treating diseases associated with
PT   ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT   disease and cancer -
XX
PS   Examples; Page -; 229pp; English.
XX
CC   The invention relates to the human ABC1 cholesterol transporter protein
```

```
CC   (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC   a member of the ATP-binding cassette (ABC transporter) superfamily of
CC   proteins, and plays a crucial role in cholesterol transport, particularly
CC   intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC   involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC   located on chromosome 9q31, and mutations in this gene are associated
CC   with two genetic HDL (high density lipoprotein) deficiency disorders,
CC   Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC   are distinguishable in that TD is an autosomal recessive disorder, while
CC   FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC   cholesterol") in the blood correlate with a high risk of cardiovascular
CC   disease, particularly coronary artery disease, but also cerebrovascular
CC   disease, coronary restenosis, and peripheral vascular disease.
CC   Conversely, a high level of HDL has protective effects against
CC   cardiovascular disease. The invention provides genetic constructs and
CC   transgenic cells and non-human animals comprising human ABC1 nucleic
CC   acids, and methods of gene therapy for the treatment or prevention of
CC   cardiovascular disease comprising the administration of an expression
CC   vector encoding ABC1 or an active fragment thereof. The invention also
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1. The
CC   present sequence represents cDNA encoding a mutant human ABC1 cholesterol
CC   transporter associated with an altered cholesterol level and therefore an
CC   altered risk of cardiovascular disease.
CC   Note: The present sequence is not shown in the specification, but is
CC   derived from the native human ABC1 cDNA shown on pages 157-160.
XX
SQ   Sequence 7864 BP; 2013 A; 1860 C; 2012 G; 1978 T; 1 other;


alignment_scores:
            Quality:  334.00              Length:     60
              Ratio:  5.567                Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
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      75 ATGGCTTGTTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 124

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     125 CAGAAGAAGACAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTAT 174

      34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     175 TTATCTTCCTGATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAA 224

      51 GlnHisGluCysHisPheProAsnLysAla 60
         |||||||||||||||||||||||||||||||
     225 CAACATGAATGCCATTTTCCAAATAAAGCC 254

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69389

seq_documentation_block:
ID   C69389 standard; cDNA; 7864 BP.
XX
AC   C69389;
XX
DT   29-JAN-2001  (first entry)
XX
DE   Human ABC1 cholesterol transporter FHA-2 mutant cDNA (C6504T).
XX
KW   Human ABC1 cholesterol transporter; chromosome 9q31;
KW   ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW   Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW   cardiovascular disease; coronary artery disease; coronary restenosis;
KW   cerebrovascular disease; peripheral vascular disease;
KW   Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
KW   X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW   prognosis; prophylaxis; drug screening; transgenic animal; mutant; ss.
XX
OS   Homo sapiens.
XX
PN   WO200055318-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-IB00532.
XX
PR   15-MAR-1999;   99US-0124702.
PR   08-JUN-1999;   99US-0138048.
PR   17-JUN-1999;   99US-0139600.
PR   01-SEP-1999;   99US-0151977.
XX
PA   (UYBR-) UNIV BRITISH COLUMBIA.
PA   (XENO-) XENON BIORESEARCH INC.
XX
PI   Hayden MR,  Wilson AR,  Pimstone SN;
XX
DR   WPI; 2000-587528/55.
DR   P-PSDB; B38108.
XX
PT   New ABC1 polypeptide is useful for treating diseases associated with
PT   ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT   disease and cancer -
XX
PS   Examples; Page -; 229pp; English.
XX
CC   The invention relates to the human ABC1 cholesterol transporter protein
CC   (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC   a member of the ATP-binding cassette (ABC transporter) superfamily of
CC   proteins, and plays a crucial role in cholesterol transport, particularly
CC   intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC   involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC   located on chromosome 9q31, and mutations in this gene are associated
CC   with two genetic HDL (high density lipoprotein) deficiency disorders,
CC   Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC   are distinguishable in that TD is an autosomal recessive disorder, while
CC   FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC   cholesterol") in the blood correlate with a high risk of cardiovascular
CC   disease, particularly coronary artery disease, but also cerebrovascular
CC   disease, coronary restenosis, and peripheral vascular disease.
CC   Conversely, a high level of HDL has protective effects against
CC   cardiovascular disease. The invention provides genetic constructs and
CC   transgenic cells and non-human animals comprising human ABC1 nucleic
CC   acids, and methods of gene therapy for the treatment or prevention of
CC   cardiovascular disease comprising the administration of an expression
CC   vector encoding ABC1 or an active fragment thereof. The invention also
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
```

```
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1. The
CC   present sequence represents cDNA encoding a mutant human ABC1 cholesterol
CC   transporter associated with an altered cholesterol level and therefore an
CC   altered risk of cardiovascular disease.
CC   Note: The present sequence is not shown in the specification, but is
CC   derived from the native human ABC1 cDNA shown on pages 157-160.
XX
SQ   Sequence 7864 BP; 2014 A; 1859 C; 2011 G; 1979 T; 1 other;


alignment_scores:
            Quality:  334.00              Length:     60
              Ratio:  5.567                Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
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 Align seg 1/1  to: C69389  from: 1  to: 7864

       1 MetAlaCysTrpProGlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPh 17
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      75 ATGGCTTGTTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 124

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     125 CAGAAGAAGACAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTAT 174

      34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     175 TTATCTTCCTGATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAA 224

      51 GlnHisGluCysHisPheProAsnLysAla 60
         |||||||||||||||||||||||||||||||
     225 CAACATGAATGCCATTTTCCAAATAAAGCC 254

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C75311

seq_documentation_block:
ID   C75311 standard; cDNA; 534 BP.
XX
AC   C75311;
XX
DT   08-FEB-2001 (first entry)
XX
DE   Human ORFX ORF866 polynucleotide sequence SEQ ID NO:1731.
XX
KW   Human; open reading frame; ORFX; detection; cytostatic; hepatotropic;
KW   vulnerary; antipsoriatic; antiparkinsonian; nootropic; neuroprotective;
KW   anticonvulsant; osteopathic; antiarthritic; immunosuppressant; cardiant;
KW   immunostimulant; thrombolytic; coagulant; vasotropic; antidiabetic;
KW   hypotensive; dermatological; immunosuppressive; antiinflammatory;
KW   antiviral; antibacterial; antifungal; antirheumatic; antithyroid;
KW   antianaemic; gene therapy; cancer; proliferative disorder; hypertension;
KW   neurodegenerative disorder; osteoarthritis; graft vs host disease;
KW   cardiovascular disease; diabetes mellitus; hypothyroidism; SCID; AIDS;
KW   cholesterol ester storage; systemic lupus erythematosus; infection;
KW   severe combined immunodeficiency; malaria; autoimmune disorder; asthma;
KW   allergy; aplastic anaemia; nocturnal haemoglobinuria; burn; wound;
KW   bone damage; cartilage damage; antiinflammatory disease; coagulation;
KW   thrombosis; contraceptive; ss.
XX
OS   Homo sapiens.
XX
PN   WO200058473-A2.
XX
PD   05-OCT-2000.
XX
PF   31-MAR-2000; 2000WO-US08621.
XX
PR   31-MAR-1999;   99US-0127607.
PR   02-APR-1999;   99US-0127636.
PR   05-APR-1999;   99US-0127728.
PR   30-MAR-2000; 2000US-0540763.
XX
PA   (CURA-) CURAGEN CORP.
XX
PI   Shimkets RA,  Leach M;
XX
DR   WPI; 2000-602362/57.
DR   P-PSDB; B41102.
XX
PT   Novel nucleic acids and peptides derived from open reading frame X,
PT   useful for treating e.g. cancers, proliferative disorders,
PT   neurodegenerative disorders and cardiovascular disease -
XX
PS   Claim 5; Page 1369-1370; 5507pp; English.
XX
CC   C74446 to C77606 encode the proteins given in B40237 to B43397, which
CC   represent the human ORFX open reading frames 1 to 3161. The ORFX
CC   sequences have activities such as: cytostatic; hepatotropic; vulnerary;
CC   antipsoriatic; antiparkinsonian; nootropic; neuroprotective; osteopathic;
CC   anticonvulsant; antiarthritic; immunosuppressant; immunostimulant;
CC   cardiant; thrombolytic; coagulant; vasotropic; antidiabetic; hypotensive;
CC   dermatological; immunosuppressive; antiinflammatory; antibacterial;
CC   antiviral; antifungal; antirheumatic; antithyroid; and antianaemic. The
CC   sequences can be used for determining the presence of or predisposition
CC   to, or preventing or treating pathological conditions associated with an
CC   ORFX-associated disorder. The nucleic acids can be used to express ORFX
CC   proteins in gene therapy vectors. The proteins and nucleic acids may be
CC   used to treat cancers, proliferative disorders, neurodegenerative
CC   disorders, osteoarthritis, graft vs host disease, cardiovascular disease,
CC   diabetes mellitus, hypertension, hypothyroidism, cholesterol ester
CC   storage, systemic lupus erythematosus, severe combined immunodeficiency
CC   (SCID), AIDS, viral, bacterial or fungal infection, malaria, autoimmune
CC   disorders, asthma, allergies, aplastic anaemia, burns, wounds, bone and
CC   cartilage damage, nocturnal haemoglobinuria, antiinflammatory disease; to
CC   enhance coagulation; to inhibit thrombosis; and as a contraceptive.
XX
SQ   Sequence 534 BP; 94 A; 181 C; 153 G; 106 T; 0 other;


alignment_scores:
            Quality:  230.00              Length:     59
              Ratio:  4.600                Gaps:      0
 Percent Similarity:  84.746   Percent Identity: 67.797

alignment_block:
 US-09-526-193A-1_COPY_1_60 x C75311    ..

 Align seg 1/1  to: C75311  from: 1  to: 534

       1 MetAlaCysTrpProGlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPh 17
         ||||||   |||   ||||||   ||||||||||||||||||::   ::
     199 ATGGCCTTCTGGACACAGCTGATGCTGCTGCTCTGGAAGAATTTCATGTA 248

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         :|||||||||||      |||||||||:::|||:::   ||||||||||
     249 TCGCCGGAGACAGCCGGTCCAGCTCCTGGTCGAATTGCTGTGGCCTCTCT 298

      34 heIlePheLeuIleLeuIleSerValArgLeuSerTyrProProTyrGlu 50
         ||:::|||:::||||||::::::||||||   |||:::||||||   |||
     299 TCCTCTTCTTCATCCTGGTGGCTGTTCGCCACTCCCACCCGCCCCTGGAG 348

      51 GlnHisGluCysHisPheProAsnLys 59
         :::|||||||||||||||||||||||||
     349 CACCATGAATGCCACTTCCCAAACAAG 375

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:Z94734

seq_documentation_block:
ID   Z94734 standard; cDNA; 6880 BP.
XX
AC   Z94734;
XX
DT   01-AUG-2000  (first entry)
```

```
XX
DE   Human ATP binding cassette ABCA1 (ABC1) cDNA.
XX
KW   ABCA1; ABC1; ATP binding cassette; human; cholesterol;
KW   interleukin-1 beta; transporter; inflammation; septic shock;
KW   rheumatoid arthritis; Tangier disease; hypertriglyceridemia;
KW   splenomegaly; atherosclerosis; lipid disorder; dyslipidemia;
KW   psoriasis; lupus erythematosus; diagnosis; gene therapy;
KW   chromosome 9q22-31; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             121..6726
FT                   /*tag= a
XX
PN   WO200018912-A2.
XX
PD   06-APR-2000.
XX
PF   21-SEP-1999;   99WO-EP06991.
XX
PR   25-SEP-1998;   98US-0101706.
XX
PA   (FARB ) BAYER AG.
XX
PI   Schmitz G,  Klucken J;
XX
DR   WPI; 2000-293151/25.
DR   P-PSDB; Y79380.
XX
PT   Adenosine triphosphate binding proteins useful for identifying agents
PT   for treating atherosclerosis and other inflammatory disorders -
XX
PS   Claim 9; Page 90-93; 154pp; English.
XX
CC   The present sequence is that of human cDNA encoding ATP binding
CC   cassette protein ABCA1 (ABC1, see Y79380), the human homologue of
CC   mouse ABCA1.  The cDNA was identified using a differential display
CC   method in which monocytes from peripheral blood were subjected to
CC   macrophage differentiation and cholesterol loading with acetylated
CC   low density lipoproteins and subsequent deloading with high density
CC   lipoprotein (HDL3) to identify cholesterol sensitive genes.  The
CC   ABCA1 gene maps to human chromosome 9q22-31.  Dysregulated ABCA1
CC   is the gene locus involved in the HDL deficiency syndrome
CC   Tangier disease, associated with hypertriglyceridemia and
CC   splenomegaly.  ABCA1 is also a transporter for interleukin-1 beta,
CC   making the gene a candidate for treatment of inflammatory diseases
CC   such as rheumatoid arthritis and septic shock.  The invention
CC   also provides other cholesterol-sensitive ABC genes (see Z94735-63)
CC   that can be used for diagnostic and therapeutic applications,
CC   and for biochemical or cell-based assays to screen for
CC   pharmacologically active compounds useful for the treatment of
CC   lipid disorders, atherosclerosis or other inflammatory diseases
CC   such as psoriasis and lupus erythematosus.
XX
SQ   Sequence 6880 BP; 1760 A; 1656 C; 1783 G; 1681 T; 0 other;


alignment_scores:
            Quality:  220.00              Length:     40
              Ratio:  5.500                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-526-193A-1_COPY_1_60 x Z94734   ..

 Align seg 1/1  to: Z94734  from: 1  to: 6880

      21 GlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLe 37
         ||||||||||||||||||||||||||||||||||||||||||||||||||
       1 CAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTATTTATCTTCCT 50

      37 uIleLeuIleSerValArgLeuSerTyrProProTyrGluGlnHisGluC 54
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 GATCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAACAACATGAAT 100

      54 ysHisPheProAsnLysAla 60
         ||||||||||||||||||||
     101 GCCATTTTCCAAATAAAGCC 120

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C88565

seq_documentation_block:
ID   C88565 standard; DNA; 720 BP.
XX
AC   C88565;
XX
DT   02-MAR-2001  (first entry)
XX
DE   Human rod photoreceptor ABC cDNA.
XX
KW   Ribozyme; retinal degradation; retinal disease; learning; memory;
KW   amylotropic lateral sclerosis; tumour suppression; human;
KW   rod photoreceptor; ss.
XX
OS   Homo sapiens.
XX
PN   WO200066780-A2.
XX
PD   09-NOV-2000.
XX
PF   28-APR-2000; 2000WO-US11509.
XX
PR   30-APR-1999;   99US-0131942.
XX
PA   (UYFL ) UNIV FLORIDA.
XX
PI   Lewin AS,  Muzyczka N,  Hauswirth WW,  Teschendorf C,  Burger C;
XX
DR   WPI; 2000-687548/67.
XX
PT   Novel methods for identifying genes with selected functions comprising
PT   contacting genes with a library of ribozymes, useful for identifying
PT   genes involved in, e.g. retinal disease, learning or memory and tumor
PT   suppression -
XX
PS   Disclosure; Fig 29; 111pp; English.
XX
CC   The present invention relates to a method for identifying a gene with a
CC   selected function comprising contacting genes with a library of ribozymes
CC   and identifying at least 1 ribozyme that alters the selected function of
CC   the gene. The present sequence is human rod ABCR cDNA, which was used to
CC   design ribozymes for use in the present invention. The methods (and
CC   ribozymes) are useful for identifying novel genes involved in retinal
CC   degradation, retinal disease, learning or memory, amylotropic lateral
CC   sclerosis or tumour suppression, and for producing non-human animal
CC   models of diseases.
XX
SQ   Sequence 720 BP; 176 A; 190 C; 172 G; 182 T; 0 other;


alignment_scores:
            Quality:  180.00              Length:     55
              Ratio:  3.830                 Gaps:      0
 Percent Similarity:  85.455   Percent Identity: 56.364

alignment_block:
 US-09-526-193A-1_COPY_1_60 x C88565   ..

 Align seg 1/1  to: C88565  from: 1  to: 720

       6 GlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGlnTh 22
         |||::::::|||||||||||||||||||   |||:::|||:::||||||
      97 CAGATACAGCTTTTGCTCTGGAAGAACTGGACCCTGCGGAAAAGGCAAAA 146
```

```
      22 rCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleL 39
         :::::::::::::|||::::::|||||||||   :::|||||||:::|
     147 GATTCGCTTTGTGGTGGAACTCGTGTGGCCTTTATCTTTATTTCTGGTCT 196

      39 euIleSerValArgLeuSerTyrProProTyrGluGlnHisGluCysHis 55
         |||||   :::|||   :::   |||   |||::::::|||||||||||||
     197 TGATCTGGTTAAGGAATGCCAACCCGCTCTACAGCCATCATGAATGCCAT 246

      56 PheProAsnLysAla 60
         ||||||||||||||||
     247 TTCCCCAACAAGGCG 261

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:Z94746

seq_documentation_block:
ID   Z94746 standard; cDNA; 7323 BP.
XX
AC   Z94746;
XX
DT   01-AUG-2000  (first entry)
XX
DE   Human ATP binding cassette ABCA5 cDNA.
XX
KW   ABCA5; ATP binding cassette; human; cholesterol; lipid disorder;
KW   atherosclerosis; lipid disorder; dyslipidemia; psoriasis;
KW   lupus erythematosus; diagnosis; gene therapy; chromosome 17q21-25;
KW   ss.
XX
OS   Homo sapiens.
XX
PN   WO200018912-A2.
XX
PD   06-APR-2000.
XX
PF   21-SEP-1999;   99WO-EP06991.
XX
PR   25-SEP-1998;   98US-0101706.
XX
PA   (FARB ) BAYER AG.
XX
PI   Schmitz G,  Klucken J;
XX
DR   WPI; 2000-293151/25.
XX
PT   Adenosine triphosphate binding proteins useful for identifying agents
PT   for treating atherosclerosis and other inflammatory disorders -
XX
PS   Claim 9; Page 126-129; 154pp; English.
XX
CC   The present sequence is that of human ATP binding cassette
CC   subfamily A protein ABCA5 cDNA.  The cDNA was identified using a
CC   differential display method in which monocytes from peripheral
CC   blood were subjected to macrophage differentiation and cholesterol
CC   loading with acetylated low density lipoproteins and subsequent
CC   deloading with high density lipoprotein (HDL3) to identify
CC   cholesterol sensitive genes.  The gene maps to chromosome 17q21-25.
CC   The invention provides cholesterol-sensitive ABC genes (see
CC   Z94734-63).  These genes, and polypeptides encoded by them,
CC   can be used for diagnostic and therapeutic applications, and for
CC   biochemical or cell-based assays to screen for pharmacologically
CC   active modulator compounds useful for the treatment of lipid
CC   disorders, atherosclerosis or other inflammatory diseases such as
CC   psoriasis and lupus erythematosus.
XX
SQ   Sequence 7323 BP; 1796 A; 1976 C; 1853 G; 1698 T; 0 other;


alignment_scores:
            Quality:  180.00              Length:     55
              Ratio:  3.830                Gaps:      0
  Percent Similarity:  85.455   Percent Identity: 56.364

alignment_block:
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 US-09-526-193A-1_COPY_1_60 x Z94746   ..

 Align seq 1/1  to: Z94746  from: 1  to: 7323

       6 GlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGlnTh 22
         |||:::::::|||||||||||||||||||   |||:::|||:::|||||
     103 CAGATACAGCTTTTGCTCTGGAAGAACTGGACCCTGCGGAAAAGGCAAAA 152

      22 rCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleL 39
         :::::::::::::|||::::::|||||||||   :::|||||||:::|
     153 GATTCGCTTTGTGGTGGAACTCGTGTGGCCTTTATCTTTATTTCTGGTCT 202

      39 euIleSerValArgLeuSerTyrProProTyrGluGlnHisGluCysHis 55
         |||||   :::|||   :::   |||   |||::::::|||||||||||||
     203 TGATCTGGTTAAGGAATGCCAACCCGCTCTACAGCCATCATGAATGCCAT 252

      56 PheProAsnLysAla 60
         ||||||||||||||||
     253 TTCCCCAACAAGGCG 267

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA1998.DAT:V33392

seq_documentation_block:
ID   V33392 standard; DNA; 7784 BP.
XX
AC   V33392;
XX
DT   27-JAN-1999  (first entry)
XX
DE   ATP binding cassette transporter, ABCR, coding sequence.
XX
KW   ATP binding cassette; ABC transporter; ABCR; Stargardt Disease; therapy;
KW   Fundus Flavimaculatus; age-related macular degeneration; diagnosis; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             590..7411
FT                   /*tag=  a
XX
PN   WO9837764-A1.
XX
PD   03-SEP-1998.
XX
PF   27-FEB-1998;   98WO-US03895.
XX
PR   27-FEB-1997;   97US-0039388.
XX
PA   (BAYU ) BAYLOR COLLEGE MEDICINE.
PA   (UYJO ) UNIV JOHNS HOPKINS.
PA   (UTAH ) UNIV UTAH.
PA   (USSH ) US DEPT HEALTH & HUMAN SERVICES.
XX
PI   Allikmets R,  Anderson KL,  Dean M,  Leppart M,  Lewis RA;
PI   Li Y,  Lupski JR,  Nathans J,  Rattner A,  Shroyer NF;
PI   Singh N,  Smallwood PM,  Sun H;
XX
DR   WPI; 1998-495375/42.
DR   P-PSDB; W70398.
XX
PT   Retina-specific ATP-binding cassette transporter and DNA - useful
PT   for, e.g. diagnosis and treatment of macular degeneration, such as
PT   in Stargardt Disease, Fundus Flavimaculatus and age-related
PT   degeneration
XX
PS   Claim 2; Fig 3; 79pp; English.
XX
CC   This sequence encodes the human retina specific ATP binding cassette
CC   transporter (ABCR) of the invention. ABCR may be used in compositions for
CC   screening agents that alters ABCR. The agent can inhibit Stargardt
CC   Disease, Fundus Flavimaculatus and age-related macular degeneration (MD).
CC   Primers and probes for the ABCR DNA can be used in a diagnostic kit for
CC   detecting MD.
```

```
XX
SQ   Sequence 7784 BP; 1903 A; 2104 C; 1967 G; 1810 T; 0 other;


alignment_scores:
            Quality:  180.00              Length:     55
              Ratio:  3.830                Gaps:      0
 Percent Similarity:  85.455   Percent Identity: 56.364

alignment_block:
 US-09-526-193A-1_COPY_1_60 x V33392   ..

 Align seg 1/1  to: V33392  from: 1  to: 7784

       6 GlnLeuArgLeuLeuLeuTrpLysAsnLeuThrPheArgArgArgGlnTh 22
         |||::::::|||||||||||||||||||   |||:::|||:::||||||
     605 CAGATACAGCTTTTGCTCTGGAAGAACTGGACCCTGCGGAAAAGGCAAAA 654

      22 rCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuIleL 39
            ::::::::::::|||::::::|||||||||   :::|||||||:::|
     655 GATTCGCTTTGTGGTGGAACTCGTGTGGCCTTTATCTTTATTTCTGGTCT 704

      39 euIleSerValArgLeuSerTyrProProTyrGluGlnHisGluCysHis 55
         |||||   :::|||   :::   |||   |||::::::|||||||||||||
     705 TGATCTGGTTAAGGAATGCCAACCCGCTCTACAGCCATCATGAATGCCAT 754

      56 PheProAsnLysAla 60
         |||||||||||||||
     755 TTCCCCAACAAGGCG 769

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69133

seq_documentation_block:
ID   C69133 standard; DNA; 4736 BP.
XX
AC   C69133;
XX
DT   29-JAN-2001  (first entry)
XX
DE   Human ABC1 gene exon 2.
XX
KW   Human ABC1 cholesterol transporter; chromosome 9q31;
KW   ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW   Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW   cardiovascular disease; coronary artery disease; coronary restenosis;
KW   cerebrovascular disease; peripheral vascular disease;
KW   Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
KW   X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW   prognosis; prophylaxis; drug screening; transgenic animal; ds.
XX
OS   Homo sapiens.
XX
PN   WO200055318-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-IB00532.
XX
PR   15-MAR-1999;   99US-0124702.
PR   08-JUN-1999;   99US-0138048.
PR   17-JUN-1999;   99US-0139600.
PR   01-SEP-1999;   99US-0151977.
XX
PA   (UYBR-) UNIV BRITISH COLUMBIA.
PA   (XENO-) XENON BIORESEARCH INC.
XX
PI   Hayden MR,  Wilson AR,  Pimstone SN;
XX
DR   WPI; 2000-587528/55.
XX
PT   New ABC1 polypeptide is useful for treating diseases associated with
PT   ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT   disease and cancer -
XX
PS   Disclosure; Fig 12; 229pp; English.
XX
CC   The invention relates to the human ABC1 cholesterol transporter protein
CC   (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC   a member of the ATP-binding cassette (ABC transporter) superfamily of
CC   proteins, and plays a crucial role in cholesterol transport, particularly
CC   intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC   involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC   located on chromosome 9q31, and mutations in this gene are associated
CC   with two genetic HDL (high density lipoprotein) deficiency disorders,
CC   Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC   are distinguishable in that TD is an autosomal recessive disorder, while
CC   FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC   cholesterol") in the blood correlate with a high risk of cardiovascular
CC   disease, particularly coronary artery disease, but also cerebrovascular
CC   disease, coronary restenosis, and peripheral vascular disease.
CC   Conversely, a high level of HDL has protective effects against
CC   cardiovascular disease. The invention provides genetic constructs and
CC   transgenic cells and non-human animals comprising human ABC1 nucleic
CC   acids, and methods of gene therapy for the treatment or prevention of
CC   cardiovascular disease comprising the administration of an expression
CC   vector encoding ABC1 or an active fragment thereof. The invention also
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1.
CC   The present sequence represents a fragment of the human ABC1 gene
CC   comprising exonic sequences.
XX
SQ   Sequence 4736 BP; 1309 A; 952 C; 972 G; 1500 T; 3 other;


alignment_scores:
            Quality:  176.50              Length:     50
              Ratio:  4.645                Gaps:      1
 Percent Similarity:  76.000   Percent Identity: 70.000

alignment_block:
 US-09-526-193A-1_COPY_1_60 x C69133   ..

 Align seg 1/1  to: C69133  from: 1  to: 4736

      12 TrpLysAsnLeuThrPheArgArgArgGln..................... 21
         |||   ::::::   |||   :::   |||
    4205 TGGATATCCATATTATTTTTAAATTTACAGTGTTCTATCTTATTTCCCAC 4254

      22 .ThrCysGlnLeuLeuLeuGluValAlaTrpProLeuPheIlePheLeuI 38
          ||||||||||||||||||||||||||||||||||||||||||||||||||
    4255 TCAGTGTCAGCTGCTGCTGGAAGTGGCCTGGCCTCTATTTATCTTCCTGA 4304

      38 leLeuIleSerValArgLeuSerTyrProProTyrGluGlnHisGluCys 54
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    4305 TCCTGATCTCTGTTCGGCTGAGCTACCCACCCTATGAACAACATGAATGT 4354

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA2000.DAT:C69132

seq_documentation_block:
ID   C69132 standard; DNA; 10545 BP.
XX
AC   C69132;
XX
DT   29-JAN-2001  (first entry)
XX
```

```
DE   Human ABC1 gene exon 1 (promoter).
XX
KW   Human ABC1 cholesterol transporter; chromosome 9q31; promoter;
KW   ATP-binding cassette; HDL deficiency disorder; high density lipoprotein;
KW   Tangier disease; TD; familial HDL deficiency; FHA; polymorphism;
KW   cardiovascular disease; coronary artery disease; coronary restenosis;
KW   cerebrovascular disease; peripheral vascular disease;
KW   Alzheimer's disease; Niemann-Pick disease; Huntington's disease;
KW   X-linked adrenoleukodystrophy; cancer; gene therapy; genetic diagnosis;
KW   prognosis; prophylaxis; drug screening; transgenic animal; ss.
XX
OS   Homo sapiens.
XX
PN   WO200055318-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-IB00532.
XX
PR   15-MAR-1999;   99US-0124702.
PR   08-JUN-1999;   99US-0138048.
PR   17-JUN-1999;   99US-0139600.
PR   01-SEP-1999;   99US-0151977.
XX
PA   (UYBR-) UNIV BRITISH COLUMBIA.
PA   (XENO-) XENON BIORESEARCH INC.
XX
PI   Hayden MR,  Wilson AR,  Pimstone SN;
XX
DR   WPI; 2000-587528/55.
XX
PT   New ABC1 polypeptide is useful for treating diseases associated with
PT   ABC1 biological activity, e.g. Alzheimer's disease, Huntington's
PT   disease and cancer -
XX
PS   Claim 50; Fig 12; 229pp; English.
XX
CC   The invention relates to the human ABC1 cholesterol transporter protein
CC   (B38082) and to nucleic acid sequences (C69120) which encode it. ABC1 is
CC   a member of the ATP-binding cassette (ABC transporter) superfamily of
CC   proteins, and plays a crucial role in cholesterol transport, particularly
CC   intracellular cholesterol trafficking in monocytes and fibroblasts, being
CC   involved in cholesterol efflux from the cell. The gene encoding ABC1 is
CC   located on chromosome 9q31, and mutations in this gene are associated
CC   with two genetic HDL (high density lipoprotein) deficiency disorders,
CC   Tangier disease (TD) and familial HDL deficiency (FHA). These diseases
CC   are distinguishable in that TD is an autosomal recessive disorder, while
CC   FHA is inherited as an autosomal dominant trait. Low levels of HDL ("good
CC   cholesterol") in the blood correlate with a high risk of cardiovascular
CC   disease, particularly coronary artery disease, but also cerebrovascular
CC   disease, coronary restenosis, and peripheral vascular disease.
CC   Conversely, a high level of HDL has protective effects against
CC   cardiovascular disease. The invention provides genetic constructs and
CC   transgenic cells and non-human animals comprising human ABC1 nucleic
CC   acids, and methods of gene therapy for the treatment or prevention of
CC   cardiovascular disease comprising the administration of an expression
CC   vector encoding ABC1 or an active fragment thereof. The invention also
CC   encompasses compounds which mimic ABC1 activity, compounds which
CC   stimulate ABC1 expression and methods of screening for such compounds.
CC   It further relates to methods for determining whether a patient has an
CC   increased risk for cardiovascular disease due to polymorphisms in the
CC   ABC1 gene. Human ABC1 proteins and nucleotides can be used to treat
CC   or prevent cardiovascular disease, especially coronary artery disease,
CC   cerebrovascular disease, coronary restenosis or peripheral vascular
CC   disease. They may also be used in the treatment of diseases associated
CC   with ABC1 biological activity, such as Alzheimer's disease, Niemann-Pick
CC   disease, Huntington's disease, X-linked adrenoleukodystrophy and cancer.
CC   The invention specifically excludes proteins with the exact amino acid
CC   sequences of GenBank Accession No: CAA10005.1 and X75926, and the nucleic
CC   acid with the exact sequence as GenBank Accession No: AJ012376.1. The
CC   present sequence represents the human ABC1 gene promoter region (exon 1).
XX
SQ   Sequence 10545 BP; 2647 A; 2225 C; 2411 G; 3256 T; 6 other;

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    8234 ATGGCTTGTTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCACTTT 8283

      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         ||||||||||||||||   :::|||   ::::::::::|||         :
    8284 CAGAAGAAGACAAACAGTAAGCTTGGGTTTTTCAGCAGCGGGGGGTTCTC 8333

      34 heIlePhe 36
         ::|||||
    8334 TCATTTTT 8341

seq_name: /SIDS6/gcgdata/geneseq/geneseqn/NA1998.DAT:V16345

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XX
AC   V16345;
XX
DT   03-JUN-1998  (first entry)
XX
DE   cDNA encoding full length human ATP binding cassette transporter.
XX
KW   Human; netrin; hNET; ATP binding cassette transporter; hABC3;
KW   ribosomal L3; RPL3L; augmenter of liver regeneration; hALR; treatment;
KW   trapping; modulation; expression; antibody; identification; binding;
KW   cystic fibrosis; transport; substrate specificity; ligand; exon trap; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   CDS             573..5687
FT                   /*tag= a
FT                   /product= ABC transporter
XX
PN   WO9748797-A1.
XX
PD   24-DEC-1997.
XX
PF   16-JAN-1997;   97WO-US00785.
XX
PR   09-DEC-1996;   96US-0762500.
PR   17-JUN-1996;   96US-0665259.
PR   01-OCT-1996;   96US-0720614.
XX
PA   (GENZ ) GENZYME CORP.
XX
PI   Burn TC,  Connors TD,  Dackowski WR,  Klinger KW,  Landes GM;
PI   Van Raay TJ;
XX
DR   WPI; 1998-063138/06.
DR   P-PSDB; W46771.
XX
PT   Human chromosome 16 genes encoding netrin, ATP binding cassette
PT   transporter, ribosomal L3 and augmenter of liver regeneration
PT   proteins - useful for, e.g. treatment of liver disease and cystic
PT   fibrosis
XX
PS   Claim 33; Fig 15A-J; 220pp; English.
XX
CC   The present sequence encodes human ATP binding cassette transporter
```

```
CC   (ABC). The ABC gene is located in the PKD1 locus, between the LCN1 and
CC   D16s291 markers in a centromeric to telomeric orientation. The sequence
CC   shows homology with murine ABC1 and ABC2 genes. The ABC proteins are
CC   responsible for the transport of a wide variety of substrates across
CC   cell membranes. Proteins in this family are linked by strong structural
CC   similarities. ABC transporters govern unidirectional transport of
CC   molecules into or out of cells and across subcellular membranes. The
CC   sequence was isolated using an exon trap. Sequences encoding human netrin
CC   (hNET), human ribosomal L3 (RPL3L), and human augmenter of liver
CC   regeneration (hALR) were also isolated. The antisense oligonucleotides of
CC   the present sequence are used to modulate expression of ABC prevent its
CC   translation. Antibodies against ABC can be used to block binding of its
CC   naturally occurring ligands. Host cells containing vectors with DNA
CC   inserts encoding the protein can be used in a method for identifying
CC   compounds which bind to ABC. Modulation or alteration of hABC3 substrate
CC   specificity may have significant therapeutic implications for cystic
CC   fibrosis.
XX
SQ   Sequence 6525 BP; 1333 A; 2026 C; 1859 G; 1307 T; 0 other;


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      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         :::::::|||:::::::         :::||||||||::      ||||||:
     623 GCAGAAGCGGAAGGTCCTGGTGACGGTCCTGGAACTCTTCCTGCCATTGC 672

      34 heIlePheLeuIleLeuIleSerValArgLeu 44
         :::::      |||||||||   :::|||||||
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seq_documentation_block:
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XX
AC   Z94761;
XX
DT   01-AUG-2000  (first entry)
XX
DE   Human ATP binding cassette ABCA3 (ABC3) cDNA.
XX
KW   ABCA3; ABC3; ATP binding cassette; human; cholesterol; lipid disorder;
KW   atherosclerosis; lipid disorder; dyslipidemia; psoriasis;
KW   lupus erythematosus; diagnosis; gene therapy; MRP4;
KW   multidrug resistance associated protein; chromosome 16p13.3; ss.
XX
OS   Homo sapiens.
XX
PN   WO200018912-A2.
XX
PD   06-APR-2000.
XX
PF   21-SEP-1999;   99WO-EP06991.
XX
PR   25-SEP-1998;   98US-0101706.
XX
PA   (FARB ) BAYER AG.
XX
PI   Schmitz G,  Klucken J;
XX
DR   WPI; 2000-293151/25.
XX
PT   Adenosine triphosphate binding proteins useful for identifying agents
PT   for treating atherosclerosis and other inflammatory disorders -
XX
PS   Claim 9; Page 140-142; 154pp; English.
XX
CC   The present sequence is that of human ATP binding cassette
CC   subfamily A protein ABCA3 cDNA.  The cDNA was identified using a
CC   differential display method in which monocytes from peripheral
CC   blood were subjected to macrophage differentiation and cholesterol
CC   loading with acetylated low density lipoproteins and subsequent
CC   deloading with high density lipoprotein (HDL3) to identify
CC   cholesterol sensitive genes.  The gene maps to chromosome 16p13.3.
CC   The invention provides cholesterol-sensitive ABC genes (see
CC   Z94734-63).  These genes, and polypeptides encoded by them,
CC   can be used for diagnostic and therapeutic applications, and for
CC   biochemical or cell-based assays to screen for pharmacologically
CC   active modulator compounds useful for the treatment of lipid
CC   disorders, atherosclerosis or other inflammatory diseases such as
CC   psoriasis and lupus erythematosus.
XX
SQ   Sequence 6491 BP; 1304 A; 2025 C; 1858 G; 1304 T; 0 other;


alignment_scores:
           Quality:   84.00            Length:     44
             Ratio:  2.710              Gaps:      0
 Percent Similarity:  70.455   Percent Identity: 47.727

alignment_block:
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      17 eArgArgArgGlnThrCysGlnLeuLeuLeuGluValAlaTrpProLeuP 34
         :::::::|||::::::         :::|||||||:::      ||||||:
     610 GCAGAAGCGGAAGGTCCTGGTGACGGTCCTGGAACTCTTCCTGCCATTGC 659

      34 heIlePheLeuIleLeuIleSerValArgLeu 44
         :::::      |||||||||   :::|||||||
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Date: Jun 2, 2001  8:11 PM

About: Results were produced by the GenCore software, version 4.5,
       Copyright (c) 1993-2000 Compugen Ltd.

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gb_pr5:AK024328         +   334.00  767.92  1.5e-34  1556   ! AK024328 Homo sapiens cDNA FLJ
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gb_pat1:AX060721        +   334.00  750.93  1.3e-33 10474   ! AX060721 Sequence 9 from Pate
gb_pat1:AX060898        +   334.00  750.93  1.3e-33 10474   ! AX060898 Sequence 7 from Pate
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gb_ro1:MMABC1           +   321.00  722.68  4.9e-32  7878   ! X75926 Mus musculus mRNA for A
gb_pr4:AF250238         +   230.00  508.73  4.0e-20  6588   ! AF250238 Homo sapiens macropha
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gb_pat1:AX059973        +   220.00  481.78  1.3e-18  9497   ! AX059973 Sequence 91 from Pate
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gb_pat1:AX059976        +   220.00  481.69  1.3e-18  9593   ! AX059976 Sequence 94 from Pate
gb_ro1:MMAF000149       +   185.00  401.26  3.9e-14  7268   ! AF000149 Mus musculus ATP-bind
gb_pat1:AX048329        +   180.00  410.02  1.3e-14   720   ! AX048329 Sequence 65 from Paten
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gb_pr4:AF001945         +   180.00  389.38  1.8e-13  7298   ! AF001945 Homo sapiens rim ABC
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gb_om:BTU90126          +   179.00  386.53  2.6e-13  7709   ! U90126 Bos taurus ABC transpor
gb_ro1:AF287263         +   177.00  349.82  2.9e-11 278572   ! AF287263 Mus musculus ATP-bi
gb_pr4:AF275948         +   176.50  354.21  1.6e-11 149034   ! AF275948 Homo sapiens ABCA1
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gb_htg16:AC073805       -   153.50  297.11  2.5e-08 200143   ! AC073805 Mus musculus clone
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gb_pr4:AF178941         +   103.00  206.12  0.0029   8056   ! AF178941 Homo sapiens ATP-bind
gb_ro1:MMABC2           +   102.00  204.24  0.0037   7629   ! X75927 Mus musculus mRNA for A
gb_ro1:AB037937         +   102.00  203.77  0.0039   8040   ! AB037937 Rattus norvegicus mRN
gb_htg6:AC018113        -   100.00  189.28  0.0251  24018   ! AC018113 Drosophila melano
gb_htg3:AC011707        +   100.00  171.41  0.2487 178512   ! AC011707 Drosophila melan
gb_in1:AE003569         +   100.00  167.04  0.4354 291414   ! AE003569 Drosophila melan
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DEFINITION  Homo sapiens mRNA for ABC1, partial cds.
ACCESSION   AB037924
VERSION     AB037924.1  GI:9711458
KEYWORDS    ABC1.
SOURCE      Homo sapiens placenta cDNA to mRNA.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (sites)
  AUTHORS   Zhao,L.X., Zhou,C.J., Tanaka,A., Nakata,M., Hirabayashi,T.,
            Amachi,T., Shioda,S., Ueda,K. and Inagaki,N.
  TITLE     Cloning, characterization and tissue distribution of the rat
            ATP-binding cassette (ABC) transporter ABC2/ABCA2
  JOURNAL   Biochem. J. 350 (Pt 3), 865-872 (2000)
   PUBMED   10970803
REFERENCE   2  (bases 1 to 298)
  AUTHORS   Ueda,K., Kioka,N. and Tanaka,A.
  TITLE     Direct Submission
  JOURNAL   Submitted (02-FEB-2000) to the DDBJ/EMBL/GenBank databases.
            Kazumitsu Ueda, Kyoto University Graduate School of Agriculture,
            Division of Applied Life Sciences; Kitashirakawa, Sakyo-ku, Kyoto,
            kyoto 606-8502, Japan (E-mail:uedak@kais.kyoto-u.ac.jp,
            Tel:81-75-753-6105, Fax:81-75-753-6104)
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seq_documentation_block:
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DEFINITION  Homo sapiens ATP binding cassette transporter 1 (ABCA1) mRNA,
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ACCESSION   AF258627
VERSION     AF258627.1  GI:7769707
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 697)
  AUTHORS   Pullinger,C.R., Hakamata,H., Duchateau,P.N., Eng,C.,
            Aouizerat,B.E., Fielding,C.J. and Kane,J.P.
  TITLE     Analysis of hABC1 gene 5' end: additional peptide sequence,
            promoter region, and four polymorphisms
  JOURNAL   Biochem. Biophys. Res. Commun. 271 (2000) In press
REFERENCE   2  (bases 1 to 697)
  AUTHORS   Pullinger,C.R., Hakamata,H., Duchateau,P.N., Eng,C.,
            Aouizerat,B.E., Fielding,C.J. and Kane,J.P.
  TITLE     Direct Submission
  JOURNAL   Submitted (19-APR-2000) Cardiovascular Research Institute,
            University of California, San Francisco, 505 Parnassus Avenue, San
            Francisco, CA 94143-0130, USA
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                     /chromosome="9"
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                     /tissue_type="placenta"
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                     /note="membrane-bound"
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                     /db_xref="GI:7769708"
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ORIGIN


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     446 CAGAAGAAGACAAACATGTCAGCTGCTGCTGGAAGTGGCCTGGCCTCTAT 495

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DEFINITION  Homo sapiens cDNA FLJ14266 fis, clone PLACE1002437, highly similar
            to ATP-BINDING CASSETTE TRANSPORTER 1.
ACCESSION   AK024328
VERSION     AK024328.1  GI:10436685
KEYWORDS    oligo capping; fis (full insert sequence).
SOURCE      Homo sapiens placenta cDNA to mRNA, clone_lib:PLACE1
            clone:PLACE1002437.
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            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (sites)
  AUTHORS   Isogai,T., Ota,T., Hayashi,K., Sugiyama,T., Otsuki,T., Suzuki,Y.,
            Nishikawa,T., Nagai,K., Sugano,S., Takahashi-Fujii,A., Hara,H.,
            Tanase,T., Nomura,Y., Togiya,S., Komai,F., Hara,R., Takeuchi,K.,
            Arita,M., Nabekura,T., Ishii,S., Kawai,Y., Saito,K., Yamamoto,J.,
            Wakamatsu,A., Nakamura,Y., Nagahari,K., Masuho,Y. and Oshima,A.
  TITLE     NEDO human cDNA sequencing project
  JOURNAL   Unpublished (2000)
REFERENCE   2  (bases 1 to 1556)
  AUTHORS   Isogai,T. and Otsuki,T.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-AUG-2000) to the DDBJ/EMBL/GenBank databases. Takao
            Isogai, Helix Research Institute, Genomics Laboratory; 1532-3 Yana,
            Kisarazu, Chiba 292-0812, Japan (E-mail:genomics@hri.co.jp,
            Tel:81-438-52-3951, Fax:81-438-52-3952)
COMMENT     NEDO human cDNA sequencing project supported by Ministry of
            International Trade and Industry of Japan; cDNA full insert
            sequencing: Research Association for Biotechnology; cDNA library
            construction, 5'- & 3'-end one pass sequencing and clone selection:
            Helix Research Institute (supported by Japan Key Technology Center
            etc.) and Department of Virology, Institute of Medical Science,
            University of Tokyo.
FEATURES             Location/Qualifiers
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seq_name: gb_pat1:AX060713

seq_documentation_block:
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DEFINITION  Sequence 1 from Patent WO0078972.
ACCESSION   AX060713
VERSION     AX060713.1  GI:12406103
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 10442)
  AUTHORS   Lawn,R.M., Wade,D. and Garvin,M.
  TITLE     Regulation with binding cassette transporter protein abc1
  JOURNAL   Patent: WO 0078972-A 1 28-DEC-2000;
            CV THERAPEUTICS, INC. (US)
FEATURES             Location/Qualifiers
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BASE COUNT     2898 a   2297 c   2408 g   2835 t      4 others
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seq_name: gb_pat1:AX060892

seq_documentation_block:
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DEFINITION  Sequence 1 from Patent WO0078971.
ACCESSION   AX060892
VERSION     AX060892.1  GI:12406270
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 10442)
  AUTHORS   Lawn,R.M., Wade,D., Oram,J.F. and Garvin,M.
  TITLE     Atp binding cassette transporter protein abc1 polypeptides
  JOURNAL   Patent: WO 0078971-A 1 28-DEC-2000;
            CV THERAPEUTICS, INC. (US)
FEATURES             Location/Qualifiers
     source          1. .10442
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BASE COUNT     2898 a   2297 c   2408 g   2835 t      4 others
ORIGIN


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seq_name: gb_pr4:AF285167

seq_documentation_block:
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DEFINITION  Homo sapiens ATP-binding cassette transporter 1 (ABCA1) mRNA,
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ACCESSION   AF285167
VERSION     AF285167.1  GI:9755158
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
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            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 10442)
  AUTHORS   Schwartz,K., Lawn,R.M. and Wade,D.P.
  TITLE     ABCA1 gene expression and apoA-I-mediated cholesterol efflux are
            regulated by LXR
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 10442)
  AUTHORS   Lawn,R.M., Wade,D.P., Garvin,M.R., Wang,X., Schwartz,K.,
            Porter,J.G., Seilhamer,J.J., Vaughan,A.M. and Oram,J.F.
  TITLE     Direct Submission
  JOURNAL   Submitted (06-JUL-2000) Discovery Research, CV Therapeutics Inc.,
            3172 Porter Drive, Palo Alto, CA 94304, USA
FEATURES             Location/Qualifiers
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seq_name: gb_pat1:AX060719

seq_documentation_block:
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DEFINITION  Sequence 7 from Patent WO0078972.
ACCESSION   AX060719
VERSION     AX060719.1  GI:12406108
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 10474)
  AUTHORS   Lawn,R.M., Wade,D. and Garvin,M.
  TITLE     Regulation with binding cassette transporter protein abc1
  JOURNAL   Patent: WO 0078972-A 7 28-DEC-2000;
            CV THERAPEUTICS, INC. (US)
FEATURES             Location/Qualifiers
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DEFINITION  Sequence 9 from Patent WO0078972.
ACCESSION   AX060721
VERSION     AX060721.1  GI:12406109
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
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           Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
           Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 10474)
  AUTHORS   Lawn,R.M., Wade,D. and Garvin,M.
  TITLE     Regulation with binding cassette transporter protein abc1
  JOURNAL   Patent: WO 0078972-A 9 28-DEC-2000;
           CV THERAPEUTICS, INC. (US)
FEATURES             Location/Qualifiers
     source          1. .10474
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ORIGIN


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DEFINITION  Sequence 7 from Patent WO0078971.
ACCESSION   AX060898
VERSION     AX060898.1  GI:12406275
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
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           Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 10474)
  AUTHORS   Lawn,R.M., Wade,D., Oram,J.F. and Garvin,M.
  TITLE     Atp binding cassette transporter protein abc1 polypeptides
  JOURNAL   Patent: WO 0078971-A 7 28-DEC-2000;
           CV THERAPEUTICS, INC. (US)
FEATURES             Location/Qualifiers
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ORIGIN


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seq_name: gb_pat1:AX060900

seq_documentation_block:
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ACCESSION   AX060900
VERSION     AX060900.1  GI:12406276
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
           Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
           Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 10474)
  AUTHORS   Lawn,R.M., Wade,D., Oram,J.F. and Garvin,M.
  TITLE     Atp binding cassette transporter protein abc1 polypeptides
  JOURNAL   Patent: WO 0078971-A 9 28-DEC-2000;
           CV THERAPEUTICS, INC. (US)
FEATURES             Location/Qualifiers
     source          1. .10474
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ORIGIN


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DEFINITION  Mus musculus mRNA for ABC transporte (ABC1 gene).
ACCESSION   X75926
VERSION     X75926.1  GI:495256
KEYWORDS    ABC transporter; ABC1 gene; transmembrane protein.
SOURCE      house mouse.
  ORGANISM  Mus musculus
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            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 7878)
  AUTHORS   Luciani,M.F., Denizot,F., Savary,S., Mattei,M.G. and Chimini,G.
  TITLE     Cloning of two novel ABC transporters mapping on human chromosome 9
  JOURNAL   Genomics 21 (1), 150-159 (1994)
  MEDLINE   94375008
REFERENCE   2  (bases 1 to 7878)
  AUTHORS   Chimini,G.
  TITLE     Direct Submission
  JOURNAL   Submitted (05-NOV-1993) G. Chimini, Centre d'Immunologie de
            Marseille Luminy, Parc Scientifique de Luminy, 13288 Marseille,
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DEFINITION  Homo sapiens macrophage ABC transporter (ABCA7) mRNA, complete cds.
ACCESSION   AF250238
VERSION     AF250238.1  GI:9211111
KEYWORDS    .
SOURCE      human.
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REFERENCE   1  (bases 1 to 6588)
  AUTHORS   Kaminski,W.E., Orso,E., Diederich,W., Klucken,J., Drobnik,W. and
            Schmitz,G.
  TITLE     Identification of a novel human sterol-sensitive ATP-binding
            cassette transporter
  JOURNAL   Biochem. Biophys. Res. Commun. 273 (2), 532-538 (2000)
  MEDLINE   20334305
REFERENCE   2  (bases 1 to 6588)
  AUTHORS   Kaminski,W.E.
  TITLE     Direct Submission
  JOURNAL   Submitted (28-MAR-2000) Intitute for Clinical Chemistry and
            Laboratory Medicine, University of Regensburg, Franz-Josef-Strauss
            Allee 11, Regensburg 93042, Germany
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DEFINITION  Homo sapiens ABC transporter member 7 (ABCA7) mRNA, complete cds.
ACCESSION   AF328787
VERSION     AF328787.1  GI:12656650
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
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REFERENCE   1  (bases 1 to 6704)
  AUTHORS   Broccardo,C., Osorio,J., Luciani,M.-F., Lynn,S., Prades,C.,
            Shulenin,S., Arnould,I., Naudin,L., Lafargue,C., Rosier,M.,
            Jordan,B., Mattei,M.G., Dean,M., Denefle,P. and Chimini,G.
  TITLE     Comparative analysis of promoter structure and genomic organization
            of human and mouse ABCA7, a novel ABCA transporter
  JOURNAL   Cytogenet. Cell Genet. (2001) In press
REFERENCE   2  (bases 1 to 6704)
  AUTHORS   Broccardo,C., Osorio,J., Luciani,M.-F., Lynn,S., Prades,C.,
            Shulenin,S., Arnould,I., Naudin,L., Lafargue,C., Rosier,M.,
            Jordan,B., Mattei,M.G., Dean,M., Denefle,P. and Chimini,G.
  TITLE     Direct Submission
  JOURNAL   Submitted (13-DEC-2000) EGC, Aventis-Pharma, 2 Rue Gaston Cremieux,
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BASE COUNT     1117 a   2176 c   2152 g   1259 t
ORIGIN


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DEFINITION  Homo sapiens mRNA for ATP-binding cassette transporter-1 (ABC-1).
ACCESSION   AJ012376
VERSION     AJ012376.1  GI:4128032
KEYWORDS    ABC-1 gene; ATP-binding cassette transporter-1.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
            Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 6880)
  AUTHORS   Langmann,T., Klucken,J., Reil,M., Liebisch,G., Luciani,M.F.,
            Chimini,G., Kaminski,W.E. and Schmitz,G.
  TITLE     Molecular cloning of the human ATP-binding cassette transporter 1
            (hABC1): evidence for sterol-dependent regulation in macrophages
  JOURNAL   Biochem. Biophys. Res. Commun. 257 (1), 29-33 (1999)
  MEDLINE   99194549
REFERENCE   2  (bases 1 to 6880)
  AUTHORS   Langmann,T.
  TITLE     Direct Submission
  JOURNAL   Submitted (11-NOV-1998) Langmann T., Institute for Clinical
            Chemistry and Laboratory Medicine, University of Regensburg,
            Franz-Josef-Strauss-Allee 11, 93053, GERMANY
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ACCESSION   AX059978
VERSION     AX059978.1  GI:12405636
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 9495)
  AUTHORS   Denefle,P., Rosier-Montus,M.F., Arnould-Reguigne,I., Prades,C.,
            Naudin,L., Lemoine,C., Duverger,N., Assmann,G., Rust,S., Funke,H.
            and Brewer,H.B.
  TITLE     Nucleic and proteinic acids corresponding to human gene abc1
  JOURNAL   Patent: WO 0078970-A 96 28-DEC-2000;
            Aventis Pharma S.A. (FR)
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ORIGIN


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(FILE 'HOME' ENTERED AT 07:32:54 ON 05 JUN 2001)

INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, ...' ENTERED AT 07:33:09 ON 05 JUN 2001

SEA (ATP (W) BINDING (W) CASSETTE (W) 1) OR ABCA1 OR ABC1

1	FILE ADISALERTS
2	FILE ADISINSIGHT
13	FILE AGRICOLA
1	FILE AQUASCI
1	FILE BIOBUSINESS
3	FILE BIOCOMMERCE
121	FILE BIOSIS
5	FILE BIOTECHABS
5	FILE BIOTECHDS
69	FILE BIOTECHNO
23	FILE CABA
18	FILE CANCERLIT
134	FILE CAPLUS
7	FILE CIN
5	FILE CONFSCI
6	FILE DDFU
682	FILE DGENE
3	FILE DRUGNL
8	FILE DRUGU
3	FILE DRUGUPDATES
8	FILE EMBAL
94	FILE EMBASE
82	FILE ESBIOBASE
28	FILE FOMAD
6	FILE FSTA
649	FILE GENBANK
1	FILE IFIPAT
1	FILE JICST-EPLUS
41	FILE LIFESCI
109	FILE MEDLINE
35	FILE PASCAL
2	FILE PHAR
6	FILE PHIN
566	FILE PROMT
131	FILE SCISEARCH
6	FILE TOXLINE
45	FILE TOXLIT
32	FILE USPATFULL
11	FILE WPIDS
11	FILE WPINDEX

L1 QUE (ATP (W) BINDING (W) CASSETTE (W) 1) OR ABCA1 OR ABC1

FILE 'MEDLINE, AGRICOLA, CAPLUS, BIOSIS, EMBASE, WPIDS, PROMT' ENTERED AT 07:36:56 ON 05 JUN 2001

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L3 367 S L2 AND (INHIBIT? OR BIND?)
L4 211 S L3 AND (HUMAN OR SAPIEN?)
L5 101 DUP REM L4 (110 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 07:41:53 ON 05 JUN 2001
SET SMA OFF
SET SMA ON

FILE 'STNGUIDE' ENTERED AT 08:19:28 ON 05 JUN 2001

FILE 'MEDLINE' ENTERED AT 08:30:11 ON 05 JUN 2001

FILE 'STNGUIDE' ENTERED AT 08:30:17 ON 05 JUN 2001

FILE 'MEDLINE, AGRICOLA, CAPLUS, BIOSIS, EMBASE, WPIDS, PROMT' ENTERED AT 08:48:01 ON 05 JUN 2001

L6 1048 S (ATP (W) BINDING (W) CASSETTE (W) 1) OR ABCA1 OR ABC1
L7 347 S L6 AND (LIPID OR CHOLESTEROL OR LIPOPROTEIN OR HDL)
L8 163 DUP REM L7 (184 DUPLICATES REMOVED)
L9 31 S L8 NOT PY>1999

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	46	(atp adj binding adj cassette adj "1") or abca1 or abc1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2001/06/05 09:18

	Document ID	Issue Date	Pages	Title
1	US 6225525 B1	20010501	20	ATP-binding cassette transporter (ABC1) modified transgenic mice
2	US 6199100 B1	20010306	69	Interactive computer network and method of operation
3	US 6195661 B1	20010227	37	Method for locating application records in an interactive-services database
4	US 6182123 B1	20010130	47	Interactive computer network and method of operation
5	US 6083706 A	20000704	64	Inhibitors of leaderless protein export

	Document ID	Issue Date	Pages	Title
6	US 6030806 A	20000229	137	Human chromosome 16 genes, compositions, methods of making and using same
7	US 6028173 A	20000222	96	Human chromosome 16 genes, compositions, methods of making and using same
8	US 6025931 A	20000215	30	Facsimile to E-mail communication system with local interface
9	US 6023345 A	20000208	30	Facsimile to E-mail communication system with local interface
10	US 5796967 A	19980818	38	Method for presenting applications in an interactive service
11	US 5758072 A	19980526	65	Interactive computer network and method of operation
12	US 5623587 A	19970422	23	Method and apparatus for producing an electronic image
13	US 5623016 A	19970422	12	Aqueous, autocrosslinking polyurethane-vinyl hybrid dispersions
14	US 5594910 A	19970114	48	Interactive computer network and method of operation

	Document ID	Issue Date	Pages	Title
15	US 5571861 A	19961105	13	Aqueous, autocrosslinking polyurethane-vinyl hybrid dispersions
16	US 5502822 A	19960326	48	Asynchronous data transmission system
17	US 5493607 A	19960220	11	Multi-system network addressing
18	US 5426651 A	19950620	19	Method for the automatic generation of test sequences
19	US 5420222 A	19950530	19	Curable organo(poly)siloxane compositions
20	US 5347632 A	19940913	68	Reception system for an interactive computer network and method of operation
21	US 5256760 A	19931026	21	Condensation copolymers with sequenced mer structure
22	US 5245458 A	19930914	10	Optical interconnect networks
23	US 5113083 A	19920512	15	Light scattering measuring apparatus utilizing a photodetector mounted on a rotary stand

	Document ID	Issue Date	Pages	Title
24	US 4802165 A	19890131	23	Method and apparatus of debugging computer programs
25	US 4450745 A	19840529	19	Electronic musical instrument with plural tone production channels
26	US 4365532 A	19821228	21	Electronic musical instrument with plural tone production channels
27	US 4080251 A	19780321		Apparatus and method for controlling a nuclear reactor
28	US RE29543 E	19780221		Elevator control system
29	US 3943758 A	19760316		Device for determining surface strains during the measurement of inherent stresses in structural components of machines or apparatus
30	US 3864025 A	19750204		DISPLAY INSTRUMENT USING OPTICAL COLLIMATION
31	US 3802316 A	19740409		APPARATUS FOR MACHINING AN ARCUATE GROOVE
32	US 3765230 A	19731016		METHOD OF MEASURING INTRINSIC STRESSES IN STRUCTURAL COMPONENTS OF MACHINES AND APPARATUS AND DEVICES FOR PERFORMING SUCH METHOD

	Document ID	Issue Date	Pages	Title
33	JP 09212538 A	19970815		METHOD AND TOOL FOR GENERATING INDEX FOR EQUAL-LENGTH BALANCED WIRING
34	JP 56046352 A	19810427		FUNCTION KEY CONTROL SYSTEM FOR TELEGRAPHIC MESSAGE TRANSMISSION
35	DE 19946159 A1	20010625		Time-critical data communication method via communication network e.g. for speech or real-time video - using service-specified transmission criteria assigned to given communication equipment when setting up communication link via communication

	Document ID	Issue Date	Pages	Title
36	WO 200115676 A2	20010618		Treating a lower than normal high density lipoprotein-cholesterol (HDL-C) level, a higher than normal triglyceride level, or a cardiovascular disease, by administering a compound that modulates LXR- or RXR-mediated transcriptional activity
37	WO 200078972 A2	20010528		Adenosine triphosphate (ATP) binding cassette (ABC) polynucleotide, useful for the development of agents for the treatment of heart disease and other disorders associated with hypercholesterolemia and atherosclerosis

	Document ID	Issue Date	Pages	Title
38	WO 200078971 A2	20010528		Adenosine triphosphate (ATP) binding cassette protein (ABC) 1 polynucleotides and polypeptides, useful for treatment of heart disease and other disorders associated with hypercholesterolemia and
39	WO 200078970 A1	20010528		New nucleic acid and proteins from the human ABC1 gene, useful for treating and preventing diseases associated with abnormal reverse transport of cholesterol
40	WO 200055318 A2	20010618		New ABC1 polypeptide is useful for treating diseases associated with ABC1 biological activity, e.g. Alzheimer's disease, Huntington's disease and

	Document ID	Issue Date	Pages	Title
41	WO 200034461 A2	20001106		New non-human mammal comprising a non-functional endogenous ligand activated transcription factor-alpha allele, useful for screening retinoid X receptor agonists which reduce cholesterol levels or inhibit cholesterol absorption in mammals
42	WO 200024390 A1	20000925		Novel method of modulating amyloid deposition, used to treat amyloidosis, Alzheimer's disease, stroke or head injury, by administering adenosine triphosphate-binding cassette transporter or flippase blocker
43	JP 05286990 A	19931102		New macrolide antibiotics related to megalomycin(s) A,B,C1 and C2 - obtd. by incubating strain of Amycolatopsis, on medium contg.

	Document ID	Issue Date	Pages	Title
44	US 5248773 A	19930928		New steroid thioether and sulphoxide derivs. - are used for prodn. of 16-methylene steroid(s)
45	SU 741051 B	19800625		Stereoscopic print identical point recognition - by image rotation, scanning, density signal conversion, and differential movement of
46	US 4199559 A	19800422		Assaying ligands and antibodies using two chromophores - forming fluorescer-quencher pair affected by analyte

YOU HAVE REQUESTED DATA FROM 31 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 31 MEDLINE
ACCESSION NUMBER: 2000191593 MEDLINE
DOCUMENT NUMBER: 20191593 PubMed ID: 10725792
TITLE: ATP-binding cassette transporter A1 (**ABCA1**) in macrophages: a dual function in inflammation and **lipid** metabolism?.
AUTHOR: Schmitz G; Kaminski W E; Porsch-Ozcurumez M; Klucken J; Orso E; Bodzioch M; Buchler C; Drobnik W
CORPORATE SOURCE: Institute of Clinical Chemistry and Laboratory Medicine, University of Regensburg, Germany.. gerd.schmitz@klinik.uni-regensburg.de
SOURCE: PATHOBIOLOGY, (1999) 67 (5-6) 236-40.
Journal code: AF6; 9007504. ISSN: 1015-2008.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000510

AB Activated **lipid**-laden macrophages in the vascular wall are key modulators of the inflammatory processes underlying atherosclerosis. We demonstrate here that the ATP-binding cassette (ABC) transporter **ABCA1** is induced during differentiation of human monocytes into macrophages. **ABCA1** has been implicated in macrophage interleukin-1beta secretion and apoptosis. Moreover, **ABCA1** mRNA and protein levels are strongly upregulated by uptake of modified LDL and downregulated by **HDL**(3)-mediated **lipid** efflux in macrophages. Mutation analysis in patients with the classical Tangier disease (TD), a monogenetic disorder characterized by hypersplenism, macrophage accumulation and deposition of cholesteryl esters in the reticuloendothelial system, low plasma **HDL** and premature atherosclerosis, revealed deleterious mutations in their **ABCA1** gene. The localization pattern of the mutations within the **ABCA1** protein appears to determine the tropism for either the reticuloendothelial system, as seen in the classical TD phenotype, or the artery wall, as in the case of **HDL** deficiency in the absence of splenomegaly. In a comprehensive analysis of the expression and regulation of all currently known human ABC transporters, we identified additional **cholesterol**-responsive genes that are induced during monocyte differentiation into macrophages. Our results indicate a dual regulatory function for **ABCA1** in macrophage **lipid** metabolism and inflammation.

L9 ANSWER 2 OF 31 MEDLINE
ACCESSION NUMBER: 2000103559 MEDLINE
DOCUMENT NUMBER: 20103559 PubMed ID: 10638204
TITLE: Hypo- and hyper alphalipoproteinemia and genetic abnormalities in reverse **cholesterol** transport system.
AUTHOR: Matsuyama A; Yamashita S
CORPORATE SOURCE: Department of Internal Medicine and Molecular Science, Graduate School of Medicine, Osaka University.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1999 Dec) 57 (12) 2729-34. Ref: 11
Journal code: KIM; 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000309
Last Updated on STN: 20000309
Entered Medline: 20000223

AB The risk of atherosclerosis has been known to be inversely correlated with the plasma concentration of high-density **lipoprotein** (**HDL**)-**cholesterol**, and we now know **HDL** plays a protective role against atherosclerosis. The most important mechanism, by which **HDL** could exert their anti-atherogenic role, is certainly the removal of excess **cholesterol** from peripheral cells and its transport to the liver, a process commonly called "reverse **cholesterol** transport system". In this system, many proteins are

involved, i.e., **ABC1**, LCAT, CETP, HTGL and SR-BI. Abnormalities of these proteins reduce the efficacy of the system, and cause abnormalities of **HDL** and atherosclerosis. In this paper, we review the recent findings on the molecular mechanism of reverse **cholesterol** transport system, and then discuss hypo- and hyperalphalipoproteinemia, which are caused by genetic abnormalities of the key players.

L9 ANSWER 3 OF 31 MEDLINE
ACCESSION NUMBER: 2000009006 MEDLINE
DOCUMENT NUMBER: 20009006 PubMed ID: 10543661
TITLE: Role of **ABC1** gene in **cholesterol** efflux and atheroprotection.
COMMENT: Comment on: Lancet. 1999 Oct 16;354(9187):1341-6
AUTHOR: Owen J S
CORPORATE SOURCE: Department of Medicine, Royal Free and University College Medical School, University College London, UK.
SOURCE: LANCET, (1999 Oct 23) 354 (9188) 1402-3.
Journal code: L0S; 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000209
Entered Medline: 19991110

L9 ANSWER 4 OF 31 MEDLINE
ACCESSION NUMBER: 2000001430 MEDLINE
DOCUMENT NUMBER: 20001430 PubMed ID: 10533863
TITLE: Mutations in the **ABC1** gene in familial **HDL** deficiency with defective **cholesterol** efflux.
COMMENT: Comment in: Lancet. 1999 Oct 23;354(9188):1402-3
AUTHOR: Marcil M; Brooks-Wilson A; Clee S M; Roomp K; Zhang L H; Yu L; Collins J A; van Dam M; Molhuizen H O; Loubster O; Ouellette B F; Sensen C W; Fichter K; Mott S; Denis M; Boucher B; Pimstone S; Genest J Jr; Kastelein J J; Hayden M R
CORPORATE SOURCE: Xenon Bioresearch Inc, NRC Innovation Centre, Vancouver, British Columbia, Canada.
SOURCE: LANCET, (1999 Oct 16) 354 (9187) 1341-6.
Journal code: L0S; 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000209
Entered Medline: 19991119

AB BACKGROUND: A low concentration of **HDL cholesterol** is the most common **lipoprotein** abnormality in patients with premature atherosclerosis. We have shown that Tangier disease, a rare and severe form of **HDL** deficiency characterised by a biochemical defect in cellular **cholesterol** efflux, is caused by mutations in the ATP-binding-cassette (**ABC1**) gene. This gene codes for the **cholesterol**-efflux regulatory protein (CERP). We investigated the presence of mutations in this gene in patients with familial **HDL** deficiency. METHODS: Three French-Canadian families and one Dutch family with familial **HDL** deficiency were studied. Fibroblasts from the proband of each family were defective in cellular **cholesterol** efflux. Genomic DNA of each proband was used for mutation detection with primers flanking each exon of the **ABC1** gene, and for sequencing of the entire coding region of the gene. PCR and restriction-fragment length polymorphism assays specific to each mutation were used to investigate segregation of the mutation in each family, and to test for absence of the mutation in DNA from normal controls. FINDINGS: A different mutation was detected in **ABC1** in each family studied. Each mutation either created a stop codon predicted to result in truncation of CERP, or altered a conserved aminoacid residue. Each mutation segregated with low concentrations of **HDL-cholesterol** in the family, and was not observed in more than 500 control chromosomes tested. INTERPRETATION: These data show that mutations in **ABC1** are the major cause of familial **HDL** deficiency associated with defective **cholesterol** efflux, and that CERP has an essential role in the formation of **HDL**. Our findings highlight the potential of

modulation of **ABC1** as a new route for increasing **HDL** concentrations.

L9 ANSWER 5 OF 31 MEDLINE
ACCESSION NUMBER: 1999454823 MEDLINE
DOCUMENT NUMBER: 99454823 PubMed ID: 10525055
TITLE: The Tangier disease gene product **ABC1** controls the cellular apolipoprotein-mediated **lipid** removal pathway.
COMMENT: Comment in: J Clin Invest. 1999 Oct;104(8):1015-7
AUTHOR: Lawn R M; Wade D P; Garvin M R; Wang X; Schwartz K; Porter J G; Seilhamer J J; Vaughan A M; Oram J F
CORPORATE SOURCE: CV Therapeutics Inc., Palo Alto, California 94304, USA.. lawn@cvt.com
CONTRACT NUMBER: DK-02456 (NIDDK)
HL-53451 (NHLBI)
HL-55362 (NHLBI)
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1999 Oct) 104 (8) R25-31.
Journal code: HS7; 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991116
AB The **ABC1** transporter was identified as the defect in Tangier disease by a combined strategy of gene expression microarray analysis, genetic mapping, and biochemical studies. Patients with Tangier disease have a defect in cellular **cholesterol** removal, which results in near zero plasma levels of **HDL** and in massive tissue deposition of cholesteryl esters. Blocking the expression or activity of **ABC1** reduces apolipoprotein-mediated **lipid** efflux from cultured cells, and increasing expression of **ABC1** enhances it. **ABC1** expression is induced by **cholesterol** loading and cAMP treatment and is reduced upon subsequent **cholesterol** removal by apolipoproteins. The protein is incorporated into the plasma membrane in proportion to its level of expression. Different mutations were detected in the **ABC1** gene of 3 unrelated patients. Thus, **ABC1** has the properties of a key protein in the cellular **lipid** removal pathway, as emphasized by the consequences of its defect in patients with Tangier disease.

L9 ANSWER 6 OF 31 MEDLINE
ACCESSION NUMBER: 1999454806 MEDLINE
DOCUMENT NUMBER: 99454806 PubMed ID: 10525038
TITLE: **ABC1**: connecting yellow tonsils, neuropathy, and very low **HDL**.
COMMENT: Comment on: J Clin Invest. 1999 Oct;104(8):R25-31
AUTHOR: Hobbs H H; Rader D J
CORPORATE SOURCE: Departments of Internal Medicine and Molecular Genetics, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas 75229, USA.. helen.hobbs@email.swmed.edu
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1999 Oct) 104 (8) 1015-7.
Journal code: HS7; 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991116

L9 ANSWER 7 OF 31 MEDLINE
ACCESSION NUMBER: 1999383187 MEDLINE
DOCUMENT NUMBER: 99383187 PubMed ID: 10454927
TITLE: Gene linked to faulty **cholesterol** transport.
AUTHOR: Gura T
SOURCE: SCIENCE, (1999 Aug 6) 285 (5429) 814-5.
Journal code: UJ7; 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

L9 ANSWER 8 OF 31 MEDLINE
ACCESSION NUMBER: 1999364413 MEDLINE
DOCUMENT NUMBER: 99364413 PubMed ID: 10431238
TITLE: Tangier disease is caused by mutations in the gene encoding ATP-binding cassette transporter 1.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Rust S; Rosier M; Funke H; Real J; Amoura Z; Piette J C; Deleuze J F; Brewer H B; Duverger N; Denefle P; Assmann G
CORPORATE SOURCE: Institut fur Arteriosklerosеforschung an der Westfalischen Wilhelms-Universitat Munster, Germany.. Rusts@uni-muenster.de
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 352-5.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF165281; GENBANK-AF165282; GENBANK-AF165283; GENBANK-AF165284; GENBANK-AF165285; GENBANK-AF165286; GENBANK-AF165287; GENBANK-AF165288; GENBANK-AF165289; GENBANK-AF165290; GENBANK-AF165291; GENBANK-AF165292; GENBANK-AF165293; GENBANK-AF165294; GENBANK-AF165295; GENBANK-AF165296; GENBANK-AF165297; GENBANK-AF165298; GENBANK-AF165299; GENBANK-AF165300; GENBANK-AF165301; GENBANK-AF165302; GENBANK-AF165303; GENBANK-AF165304; GENBANK-AF165305; GENBANK-AF165306; GENBANK-AF165307; GENBANK-AF165308; GENBANK-AF165309; GENBANK-AF165310
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Tangier disease (TD) was first discovered nearly 40 years ago in two siblings living on Tangier Island. This autosomal co-dominant condition is characterized in the homozygous state by the absence of **HDL-cholesterol** (**HDL**-C) from plasma, hepatosplenomegaly, peripheral neuropathy and frequently premature coronary artery disease (CAD). In heterozygotes, **HDL**-C levels are about one-half those of normal individuals. Impaired **cholesterol** efflux from macrophages leads to the presence of foam cells throughout the body, which may explain the increased risk of coronary heart disease in some TD families. We report here refining of our previous linkage of the TD gene to a 1-cM region between markers D9S271 and D9S1866 on chromosome 9q31, in which we found the gene encoding human ATP cassette-binding transporter 1 (**ABC1**). We also found a change in **ABC1** expression level on **cholesterol** loading of phorbol ester-treated THP1 macrophages, substantiating the role of **ABC1** in **cholesterol** efflux. We cloned the full-length cDNA and sequenced the gene in two unrelated families with four TD homozygotes. In the first pedigree, a 1-bp deletion in exon 13, resulting in truncation of the predicted protein to approximately one-fourth of its normal size, co-segregated with the disease phenotype. An in-frame insertion-deletion in exon 12 was found in the second family. Our findings indicate that defects in **ABC1**, encoding a member of the ABC transporter superfamily, are the cause of TD.

L9 ANSWER 9 OF 31 MEDLINE
ACCESSION NUMBER: 1999364412 MEDLINE
DOCUMENT NUMBER: 99364412 PubMed ID: 10431237
TITLE: The gene encoding ATP-binding cassette transporter 1 is mutated in Tangier disease.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Bodzioch M; Orso E; Klucken J; Langmann T; Bottcher A; Diederich W; Drobnik W; Barlage S; Buchler C; Porsch-Ozcurumez M; Kaminski W E; Hahmann H W; Oette K; Rothe G; Aslanidis C; Lackner K J; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Germany.
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 347-51.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376

ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Tangier disease (TD) is an autosomal recessive disorder of **lipid** metabolism. It is characterized by absence of plasma high-density **lipoprotein** (**HDL**) and deposition of cholesteryl esters in the reticulo-endothelial system with splenomegaly and enlargement of tonsils and lymph nodes. Although low **HDL cholesterol** is associated with an increased risk for coronary artery disease, this condition is not consistently found in TD pedigrees. Metabolic studies in TD patients have revealed a rapid catabolism of **HDL** and its precursors. In contrast to normal mononuclear phagocytes (MNP), MNP from TD individuals degrade internalized **HDL** in unusual lysosomes, indicating a defect in cellular **lipid** metabolism. **HDL** -mediated **cholesterol** efflux and intracellular **lipid** trafficking and turnover are abnormal in TD fibroblasts, which have a reduced in vitro growth rate. The TD locus has been mapped to chromosome 9q31. Here we present evidence that TD is caused by mutations in **ABC1**, encoding a member of the ATP-binding cassette (ABC) transporter family, located on chromosome 9q22-31. We have analysed five kindreds with TD and identified seven different mutations, including three that are expected to impair the function of the gene product. The identification of **ABC1** as the TD locus has implications for the understanding of cellular **HDL** metabolism and reverse **cholesterol** transport, and its association with premature cardiovascular disease.

L9 ANSWER 10 OF 31 MEDLINE
ACCESSION NUMBER: 1999364411 MEDLINE
DOCUMENT NUMBER: 99364411 PubMed ID: 10431236
TITLE: Mutations in **ABC1** in Tangier disease and familial high-density **lipoprotein** deficiency.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Brooks-Wilson A; Marcil M; Clee S M; Zhang L H; Roomp K; van Dam M; Yu L; Brewer C; Collins J A; Molhuizen H O; Loubser O; Ouelette B F; Fichter K; Ashbourne-Excoffon K J; Sensen C W; Scherer S; Mott S; Denis M; Martindale D; Frohlich J; Morgan K; Koop B; Pimstone S; Kastelein J J; Hayden M R; +
CORPORATE SOURCE: Xenon Bioresearch Inc., NRC Innovation Centre, Vancouver, British Columbia, Canada.
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 336-45.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376; GENBANK-X75926
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Genes have a major role in the control of high-density **lipoprotein** (**HDL**) **cholesterol** (**HDL**-C) levels. Here we have identified two Tangier disease (TD) families, confirmed 9q31 linkage and refined the disease locus to a limited genomic region containing the gene encoding the ATP-binding cassette transporter (**ABC1**). Familial **HDL** deficiency (FHA) is a more frequent cause of low **HDL** levels. On the basis of independent linkage and meiotic recombinants, we localized the FHA locus to the same genomic region as the TD locus. Mutations in **ABC1** were detected in both TD and FHA, indicating that TD and FHA are allelic. This indicates that the protein encoded by **ABC1** is a key gatekeeper influencing intracellular **cholesterol** transport, hence we have named it **cholesterol** efflux regulatory protein (CERP).

L9 ANSWER 11 OF 31 MEDLINE
ACCESSION NUMBER: 1999364404 MEDLINE
DOCUMENT NUMBER: 99364404 PubMed ID: 10431227
TITLE: The ABCs of **cholesterol** efflux.
COMMENT: Comment on: Nat Genet. 1999 Aug;22(4):336-45
Comment on: Nat Genet. 1999 Aug;22(4):347-51
Comment on: Nat Genet. 1999 Aug;22(4):352-5
AUTHOR: Young S G; Fielding C J
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 316-8.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Commentary

News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

L9 ANSWER 12 OF 31 MEDLINE
ACCESSION NUMBER: 1999194549 MEDLINE
DOCUMENT NUMBER: 99194549 PubMed ID: 10092505
TITLE: Molecular cloning of the human ATP-binding cassette transporter 1 (hABC1): evidence for sterol-dependent regulation in macrophages.
AUTHOR: Langmann T; Klucken J; Reil M; Liebisch G; Luciani M F; Chimini G; Kaminski W E; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, 93042, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 Apr 2) 257 (1) 29-33.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990511
AB We have cloned the full-length cDNA for the human ATP binding cassette transporter 1 (hABC1). The 6603-bp open reading frame encodes a polypeptide of 2201 amino acids resulting in a deduced molecular weight of 220 kDa. The hABC1 cDNA is highly homologous (62%) to the human rim ABC transporter (ABCR). hABC1 is expressed in a variety of human tissues with highest expression levels found in placenta, liver, lung, adrenal glands, and fetal tissues. We demonstrate that the hABC1 expression is induced during differentiation of human monocytes into macrophages in vitro. In macrophages, both the hABC1 mRNA and protein expression are upregulated in the presence of acetylated low-density **lipoprotein** (AcLDL). The AcLDL-induced increase in hABC1 expression is reversed by **cholesterol** depletion mediated by the addition of high-density **lipoprotein** (HDL3). Our data, demonstrating sterol-dependent regulation of hABC1 in human monocytes/macrophages, suggest a novel role for this transporter molecule in membrane **lipid** transport. Copyright 1999 Academic Press.

L9 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:746007 CAPLUS
DOCUMENT NUMBER: 132:206037
TITLE: Role of **ABC1** gene in **cholesterol** efflux and atheroprotection
AUTHOR(S): Owen, James S.
CORPORATE SOURCE: Department of Medicine, Royal Free and University College Medical School, University College London, London, NW3 2PF, UK
SOURCE: Lancet (1999), 354(9188), 1402-1403
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 16 refs., disorders caused by ATP-binding cassette transporter 1 gene (**ABC1**) mutations, AND the **ABC1** gene product (**cholesterol** efflux regulatory protein, CERP). Mutations in **ABC1** cause plasma **HDL** deficiency and premature atherosclerosis. The proposed role of CERP in cellular **cholesterol** efflux and **HDL** maturation is outlined.
REFERENCE COUNT: 16
REFERENCE(S): (1) Becq, F; J Biol Chem 1997, V272, P2695 CAPLUS
(2) Bodzioch, M; Nat Genet 1999, V22, P347 CAPLUS
(3) Brooks-Wilson, A; Nat Genet 1999, V22, P336 CAPLUS
(4) Brown, M; Science 1986, V232, P34 CAPLUS
(5) Greaves, D; Curr Opin Lipidol 1998, V9, P425 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:728924 CAPLUS
DOCUMENT NUMBER: 132:48577

TITLE: Human ATP-binding cassette transporter 1 (**ABC1**): genomic organization and identification of the genetic defect in the original Tangier disease kindred
AUTHOR(S): Remaley, Alan T.; Rust, Stephan; Rosier, Marie; Knapper, Cathy; Naudin, Laurent; Broccardo, Cyril; Peterson, Katherine M.; Koch, Christine; Arnould, Isabelle; Prades, Catherine; Duverger, Nicholas; Funke, Harald; Assman, Gerd; Dinger, Maria; Dean, Michael; Chimini, Giovanna; Santamarina-Fojo, Silvia; Fredrickson, Donald S.; Denefle, Patrice; Brewer, H. Bryan, Jr.
CORPORATE SOURCE: National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(22), 12685-12690
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tangier disease is characterized by low serum high d. lipoproteins and a biochem. defect in the cellular efflux of lipids to high d. lipoproteins. **ABC1**, a member of the ATP-binding cassette family, recently has been identified as the defective gene in Tangier disease. The authors report here the organization of the human **ABC1** gene and the identification of a mutation in the **ABC1** gene from the original Tangier disease kindred. The organization of the human **ABC1** gene is similar to that of the mouse **ABC1** gene and other related ABC genes. The **ABC1** gene contains 49 exons that range in size from 33 to 249 bp and is over 70 kb in length. Sequence anal. of the **ABC1** gene revealed that the proband for Tangier disease was homozygous for a deletion of nucleotides 3283 and 3284 (TC) in exon 22. The deletion results in a frameshift mutation and a premature stop codon starting at nucleotide 3375. The product is predicted to encode a nonfunctional protein of 1,084 aa, which is approx. half the size of the full-length **ABC1** protein. The loss of a MnlI restriction site, which results from the deletion, was used to establish the genotype of the rest of the kindred. In summary, the authors report on the genomic organization of the human **ABC1** gene and identify a frameshift mutation in the **ABC1** gene of the index case of Tangier disease. These results will be useful in the future characterization of the structure and function of the **ABC1** gene and the anal. of addnl. **ABC1** mutations in patients with Tangier disease.
REFERENCE COUNT: 49
REFERENCE(S): (1) Allikmets, R; Gene 1998, V215, P111 CAPLUS
(2) Allikmets, R; Hum Mol Genet 1996, V5, P1649 CAPLUS
(3) Allikmets, R; Science 1997, V277, P1805 CAPLUS
(4) Andrei, C; Mol Biol Cell 1999, V10, P1463 CAPLUS
(6) Bodzioch, M; Nat Genet 1999, V22, P347 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:684452 CAPLUS
DOCUMENT NUMBER: 131:349697
TITLE: Effluxed lipids: Tangier Island's latest export
AUTHOR(S): Freeman, Mason W.
CORPORATE SOURCE: Lipid Metabolism Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(20), 10950-10952
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 32 refs. Current findings of Y. Takahashi and J.D. Smith (1999) propose a novel mechanism through which apolipoprotein A-I (apoAI) appears to remove **cholesterol** from cells, a process that is defective in individuals with Tangier disease. Recently, an ATP binding cassette transporter (**ABC1**) was shown to be mutated in patients with Tangier disease. These discoveries and their implications and inter-relationships are discussed.
REFERENCE COUNT: 32
REFERENCE(S): (1) Acton, S; Science 1996, V271, P518 CAPLUS
(2) Allikmets, R; Science 1997, V277, P1805 CAPLUS
(3) Becq, F; J Biol Chem 1997, V272, P2695 CAPLUS
(4) Bodzioch, M; Nat Genet 1999, V22, P347 CAPLUS
(5) Brooks-Wilson, A; Nat Genet 1999, V22, P336 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:674884 CAPLUS
DOCUMENT NUMBER: 132:21580
TITLE: **ABC1**: connecting yellow tonsils, neuropathy, and very low **HDL**
AUTHOR(S): Hobbs, Helen H.; Rader, Daniel J.
CORPORATE SOURCE: Departments of Internal Medicine and Molecular Genetics, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75229, USA
SOURCE: J. Clin. Invest. (1999), 104(8), 1015-1017
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 20 refs., on Tangier disease, its discovery and syndrome, and its underlying mol. defect, mutations in the ATP binding cassette transporter 1 (**ABC1**) gene. Topics discussed include: the role of **ABC1** in **cholesterol** efflux, functional implications of yellow/orange tonsils, coronary artery disease and neuropathy in Tangier disease, lowered levels of high-d. **lipoprotein** (**HDL**) **cholesterol**, low-d. **lipoprotein** **cholesterol** and elevated triglycerides, and therapeutic implications.
REFERENCE COUNT: 20
REFERENCE(S): (1) Ambudkar, S; Annu Rev Pharmacol Toxicol 1999, V39, P361 CAPLUS
(4) Bodzioch, M; Nat Genet 1999, V22, P347 CAPLUS
(5) Brooks-Wilson, A; Nat Genet 1999, V22, P336 CAPLUS
(6) Brown, M; Annu Rev Biochem 1983, V52, P223 CAPLUS
(7) Francis, G; J Clin Invest 1995, V96, P78 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:487056 CAPLUS
DOCUMENT NUMBER: 131:238599
TITLE: DNA sequencing and analysis of a 67.4 kb region from the right arm of Schizosaccharomyces pombe chromosome II reveals 28 open reading frames including the genes his5, pol5, ppa2, rip1, rpb8 and skb1
AUTHOR(S): Xiang, Zheng; Lyne, Michael H.; Wood, Valerie; Rajandream, Marie-Adele; Barrell, Barclay G.; Aves, Stephen J.
CORPORATE SOURCE: School of Biological Sciences, University of Exeter, Exeter, EX4 4QG, UK
SOURCE: Yeast (1999), 15(10A), 893-901
CODEN: YESTE3; ISSN: 0749-503X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 67 393 Bp of contiguous DNA located between markers cdc18 and cdc14 on the right arm of fission yeast chromosome II has been sequenced as part of the European Union Schizosaccharomyces pombe genome sequencing project. The complete sequence, contained in cosmid clones c15C4 and c21H7, has been detd. on both strands. Sequence anal. shows that it contains 28 open reading frames capable of coding for proteins, 16 split by one or more introns, but no tRNA, rRNA or transposon sequences. The gene d. is one per 2.4 kb. Six genes have been previously described (his5, pol5, ppa2, rip1, rpb8 and skb1) and 22 are novel. Of the novel genes, 14 have significant similarity with proteins of known function, three have similarities with proteins of unknown function and five show no extensive similarities with known proteins. Sequence similarities suggest that three of the novel genes encode ATP-dependent RNA helicases, two encode transcription factor components and others encode a G-protein, a dehydrogenase, a Rab escort protein, an **Abc1**-like protein, a lipase, an ATP-binding transport protein, an amino acid permease, an acid phosphatase and a mannosyltransferase. The sequence has been submitted to the EMBL database under entries: SPBC15C4 (Accession No. AL023290), SPBC21H7 (AL023286), SPBC14C8 (part)(AL022305) and SPBC16H5 (part)(AL022104).
REFERENCE COUNT: 20
REFERENCE(S): (1) Altschul, S; Nucleic Acids Res 1997, V25, P3389 CAPLUS
(2) Bauer, B; Mol Biol Cell 1996, V7, P1521 CAPLUS
(3) Bonfield, J; Nucleic Acids Res 1995, V23, P4992 CAPLUS
(4) Bousquet, I; EMBO J 1991, V10, P2023 CAPLUS
(5) di Rago, J; J Biol Chem 1996, V271, P15341 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 31 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1999:506445 BIOSIS
DOCUMENT NUMBER: PREV199900506445
TITLE: Mutations in transportin (**ABC1**) in Tangier disease and familial **HDL** deficiency.
AUTHOR(S): Brooks-Wilson, A. R. (1); Marcil, M. (1); Clee, S. M.; Zhang, L.-H. (1); Roomp, K. (1); van Dam, M. J.; Yu, L.; Brewer, C.; Collins, J. A. (1); Molhuizen, H.O.F.; Ouellette, B.F.F.; Sensen, C. W. (1); Martindale, D.; Frohlich, J.; Morgan, K.; Koop, B.; Pimstone, S. (1); Kastelein, J.J.P.; Genest, J., Jr.; Hayden, M. R.
CORPORATE SOURCE: (1) Xenon Bioresearch, Vancouver Canada
SOURCE: American Journal of Human Genetics, (Oct., 1999) Vol. 65, No. 4, pp. A34.
Meeting Info.: 49th Annual Meeting of the American Society of Human Genetics San Francisco, California, USA October 19-23, 1999 The American Society of Human Genetics
. ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 19 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 2001:115457 PROMT
TITLE: **ABC1** Gene indntified as target for cardiovascular disease treatments.(Brief Article)
AUTHOR(S): Petersen, Alyssa F.
SOURCE: Genetic Engineering News, (1 Sep 1999) Vol. 19, No. 15, pp. 1(3).
ISSN: 0270-6377.
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
AB Vancouver, Canada-based Xenon Bioresearch Inc. along with a consortium of international research institutions, reportedly, has identified the gene which regulates **HDL Cholesterol**.

L9 ANSWER 20 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 2000:29853 PROMT
TITLE: Gene regulates the level of **cholesterol** .(researchers in Canada and Germany identifies gene)(Brief Article)
AUTHOR(S): Toops, Diane
SOURCE: Food Processing, (Dec 1999) Vol. 60, No. 12, pp. 12.
ISSN: 0015-6523.
PUBLISHER: Putman Publishing, Co.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 121
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Researchers have identified a gene that regulates the level of KDL ("happy") **cholesterol** in the body, a key step in the drive to find new treatments for heart disease, reports Associated Press. As many as 10 labs were looking for the gene, and it was isolated separately by two independent sets of scientists, one in Canada and the other in Germany.

Subscription: $40.00 per year. Published monthly. 301 East Erie Street, Chicago, IL 60611.

L9 ANSWER 21 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:736191 PROMT
TITLE: AMERICAN HEART ASSOCIATION MEETING.
AUTHOR(S): Welch, Mary
SOURCE: BIOWORLD Today, (11 Nov 1999) Vol. 10, No. 216.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 718
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Valentis Inc. said interim Phase II data showed evidence of blood vessel formation when a non-viral vascular endothelial growth factor (VEGF 165) gene medicine was delivered via its cationic **lipid** gene delivery system.

Subscription: $1350.00 per year. Published daily (5 times a week). Box

740021, Atlanta, GA 30374.

L9 ANSWER 22 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:733538 PROMT
TITLE: CV Therapeutics' Scientist Presents Role of 'Good **Cholesterol**' Gene At American Heart Association Scientific Sessions.
SOURCE: PR Newswire, (10 Nov 1999) pp. 1876.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 655
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Latest Findings Advance Understanding of **Cholesterol** Removal Process to Reduce
THIS IS THE FULL TEXT: COPYRIGHT 1999 PR Newswire Association, Inc.

L9 ANSWER 23 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:709514 PROMT
TITLE: **ABC1** based therapy, CV Therapeutics CV Therapeutics, Incytepreclinical data.
SOURCE: R & D Focus Drug News, (25 Oct 1999) .
ISSN: 1350-1135.
PUBLISHER: IMS World Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 157
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB A gene has been isolated by CV Therapeutics, in collaboration with Incyte and Washington University (USA), which is involved in the removal of **cholesterol** from cells. The gene, **ABC1**, was discovered by genetic screening of individuals with Tangier disease. This disease is caused by mutations in the **ABC1** gene, leading to reduced high density **lipoprotein** levels and, consequently, increased risk of heart disease. Preclinical studies, reported in the October 1999 issue of the Journal of Clinical Investigation, show that modulation of **ABC1** activity effects cellular **cholesterol** efflux, and conversely the gene is modulated by cellular **cholesterol** levels. ....Researchers at Rhone-Poulenc Rorer, in collaboration with Munster University and the National Institutes of Health, also identified the **ABC1** gene in separate research.
THIS IS THE FULL TEXT: COPYRIGHT 1999 IMS World Publications Ltd.

L9 ANSWER 24 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:671190 PROMT
TITLE: CV Therapeutics Scientists Demonstrate a Novel Approach to Remove **Cholesterol** From Cells.
SOURCE: PR Newswire, (14 Oct 1999) pp. 7043.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 843
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Study Finding May Lead to New Treatments for **Cholesterol** Management to Reduce
THIS IS THE FULL TEXT: COPYRIGHT 1999 PR Newswire Association, Inc.

L9 ANSWER 25 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:576707 PROMT
TITLE: Genetic Engineering News Reports on Novel Biotech Approaches to Atherosclerosis.
SOURCE: Business Wire, (7 Sep 1999) pp. 1611.
PUBLISHER: Business Wire
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 487
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB LARCHMONT, N.Y.--(BW HealthWire)--Sept. 7, 1999--
THIS IS THE FULL TEXT: COPYRIGHT 1999 Business Wire

L9 ANSWER 26 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:567551 PROMT
TITLE: Gene Found for Tangier Disease.
SOURCE: Applied Genetics News, (August 1999) Vol. 20, No. 1.

ISSN: 0271-7107.
PUBLISHER: Business Communications Company, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 310
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Two different groups have independently identified the gene responsible for Tangier disease, a severe form of familial hypercholesteremia. One group was comprised of researchers from Rhone-Poulenc Rorer (Rhone-Poulenc Rorer, Inc., 500 Arcola Rd., Collegeville, PA 19426; Tel: 610/454-8000, Fax: 610/454-3812), the University of Munster (Germany) and the National Institutes of Health. The other group consisted of scientists from Xenon Bioresearch, Inc. (Tel: 604/822-1659, Fax: 604/822-4366), the Academic Medical Centre (Amsterdam, the Netherlands), and a large consortium of Canadian research institutions. Both teams published their results in the August 2 issue of Nature Genetics.

Subscription: $395 per year as of 1/97. Published monthly. Contact Business Communications Company, Inc., 25 Van Zant Street, Suite 13, Norwalk, CT 06855. Phone (203) 853-4266. FAX 203-853-0348.

L9 ANSWER 27 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:543643 PROMT
TITLE: **ABC1** based therapy, RPR National Institutes of Health, Rhone-PoulencRorer, Munster University isolate **cholesterol** regulation gene.
SOURCE: R & D Focus Drug News, (16 Aug 1999) .
ISSN: 1350-1135.
PUBLISHER: IMSWorld Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 126
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Rhone-Poulenc Rorer, in collaboration with the University of Munster (Germany) and the National Institutes of Health (USA), has discovered a gene which has potential for the treatment of atherosclerosis. The gene, ABC-1, was found to be defective in individuals with Tangier Disease, which is caused by reduced levels of high density **lipoprotein**. The ABC-1 gene is involved in the elimination of **cholesterol** from cells, and mutation of this gene results in aberrant high density **lipoprotein** formation.

L9 ANSWER 28 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:500651 PROMT
TITLE: **CHOLESTEROL** AIN'T ALL BAD.
AUTHOR(S): Leff, David N.
SOURCE: BIOWORLD Today, (3 Aug 1999) No. 148.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 931
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB You might suppose that Tangier disease (TD) is a North Africanailment, named after the Moroccan city of Tangiers. In fact, TD owesits name to a small sandbank called Tangier Island in the middle ofChesapeake Bay.

Subscription: $1,350 as of 1/97. Published daily. Contact American Health Consultants, 3525 Piedmont Road NE, Building 6, Ste. 400, Atlanta, Georgia 30305. Phone (404) 262-7759, Fax (404) 814-0759.

L9 ANSWER 29 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:492640 PROMT
TITLE: Discovery of Gene Responsible for Lack of `Good' **Cholesterol**.
SOURCE: PR Newswire, (3 Aug 1999) pp. 4395.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 473
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Joint Research Effort by Rhone-Poulenc Rorer, the University of Munster

L9 ANSWER 30 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:492593 PROMT
TITLE: Canadian Researchers Discover Gene Responsible For Regulation of **HDL Cholesterol** Levels.
SOURCE: PR Newswire, (3 Aug 1999) pp. 4318.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 764
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB - **ABC1** Gene Provides Target for Novel Cardiovascular Disease Treatments -
THIS IS THE FULL TEXT: COPYRIGHT 1999 PR Newswire Association, Inc.

L9 ANSWER 31 OF 31 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 91:575174 PROMT
TITLE: First foot Forward
SOURCE: Community Pharmacy, (Oct 1991) pp. 22.
ISSN: 0960-376X.
LANGUAGE: English
WORD COUNT: 342
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB A NEW company offering two innovative baby milk products has just launched into the UK.
Young Nutrition boasts a 37 year heritage via its Finnish parent company Valio: the company says that it is committed to introducing a range of scientifically researched and nutritionally sound products, which are as natural as possible. The first two products from the Young Nutrition stable are First, a ready-to-feed breast milk substitute suitable for use from birth, and Forward, a ready-to-feed follow-on milk for use from age six months. Both are based on fresh milk and are sterilised by the direct method of UHT processing, a gentle procedure which involves minimum heat treatment and leaves the products fresh tasting and wholesome, says the company.
First infant milk is a whey based milk with a fat blend largely comprising milk fat, with the remainder made up of soya oil. This means that the product's fatty acid profile is close to that of breastmilk. Optimum amounts of essential fatty acids are present in the correct proportions to each other, and **cholesterol** levels are much closer to those found in breastmilk, adds Young Nutrition.
Forward, the only ready-to-feed follow-on milk available in the UK, is fortified with iron and a range of other vitamins and minerals, and has reduced levels of protein and sodium compared with those in cows' milk.
Research among **ABC1** mothers, identified as the probable purchasers, indicated that the products scored well compared with existing brands in terms of taste, smell and appearance.
Both products are presented in 200ml cartons, retailing at 42p, packaged in outers of six. Distribution to independent pharmacies will be via the CPM sales force.
Promotion for First will be routed via the NHS and will include informational advertising in baby annuals and instructional videos and literature on the use of ready-to-feed baby milks. Forward will be supported via PR, advertorials and competitions.
The Young Nutrition company itself is also to be promoted, via a joint fund-raising venture with Great Ormond Street Hospital. Symposia and study days for health professionals are also planned.
Trade contact: Young Nutrition, tel: 0737 779622.
THIS IS THE FULL TEXT: Copyright 1991 Morgan-Grampian PLC.

L5 ANSWER 1 OF 101 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 2001:165878 PROMT
TITLE: EUROPEAN PATENT DISCLOSURES.(Brief Article)
SOURCE: BIOWORLD Today, (27 Feb 2001) Vol. 12, No. 39.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2102
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB January 3 (EP); December 28 (WO)
THIS IS THE FULL TEXT: COPYRIGHT 2001 American Health Consultants, Inc.

Subscription: $1350.00 per year. Published daily (5 times a week).

L5 ANSWER 2 OF 101 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:338360 CAPLUS
DOCUMENT NUMBER: 134:336219
TITLE: Methods for use of **ABC1** cholesterol transport protein and gene to lower serum cholesterol
INVENTOR(S): Attie, Alan D.; Cook, Mark; Gray-Keller, Mark P.; Hayden, Michael R.; Pimstone, Simon; Brooks-Wilson, Angie
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032184	A2	20010510	WO 2000-US30109	20001101

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-162803 P 19991101
US 2000-215564 P 20000630

AB Methods and compds. are disclosed for lowering serum LDL levels or serum cholesterol levels, or for reducing the transport of cholesterol from the gut to the blood or the lymph, based on the observation that a gene known as **ABC1** is necessary in order for cholesterol to be transported from the intestinal lumen into the bloodstream. Methods are also claimed for the diagnosis of alleles of the **ABC1** gene. A mutant chicken phenotype, known as the WHAM chicken, characterized by low levels of serum LDL and reduced transport of cholesterol, facilitated the discovery of this function of the **ABC1** gene. The WHAM chicken **ABC1** gene has a mutation (G265A) which results in an amino acid substitution (E89K) at a glutamate residue that is conserved between **human ABC1** protein and other vertebrates. Some mutations in the **human ABC1** gene are known to cause Tangier disease when homozygous and familial hypoalphalipoproteinemia (FHA) when heterozygous. Techniques which act to **inhibit ABC1** activity in the cells of the intestinal wall will result in lower serum cholesterol without affecting **ABC1** protein activity in other cells such as cholesterol-producing cells. The chicken, cellular assays, and cell-free assays can be used for screening **inhibitors** of **ABC1** protein activity. As an example of a cellular assay, the ability of Glyburide, a sulfonylurea compd., to **inhibit** cholesterol efflux due to **ABC1** protein activity was demonstrated.

L5 ANSWER 3 OF 101 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-244356 [25] WPIDS
CROSS REFERENCE: 2000-587528 [55]
DOC. NO. CPI: C2001-073297
TITLE: Treating a lower than normal high density lipoprotein-cholesterol (HDL-C) level, a higher than normal triglyceride level, or a cardiovascular disease, by administering a compound that modulates LXR- or RXR-mediated transcriptional activity.
DERWENT CLASS: B01 B04 D16

INVENTOR(S): BROOKS-WILSON, A R; CLEE, S M; HAYDEN, M R; PIMSTONE, S N
PATENT ASSIGNEE(S): (UYBR-N) UNIV BRITISH COLUMBIA; (XENO-N) XENON GENETICS INC
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001015676	A2	20010308	(200125)*	EN	317

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001015676	A2	WO 2000-IB1492	20000901

PRIORITY APPLN. INFO: US 2000-213958 20000623; US 1999-151977 19990901; US 2000-526193 20000315
AN 2001-244356 [25] WPIDS
CR 2000-587528 [55]
AB WO 200115676 A UPAB: 20010508

NOVELTY - A method (M1) for treating a patient diagnosed as having a lower than normal high density lipoprotein-cholesterol (HDL-C) level, a higher than normal triglyceride level, or a cardiovascular disease, comprising administering a compound that modulates LXR- or RXR-mediated transcriptional activity or **ABC1** expression or activity, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method (M2) for determining whether a candidate compound modulates **ABC1** expression, comprising:

(a) providing a nucleic acid molecule comprising an **ABC1** regulatory region or promoter linked to a reporter gene;

(b) contacting the nucleic acid molecule with the candidate compound; and

(c) measuring expression of the reporter gene, where altered reporter gene expression, relative to the reporter gene expression of a corresponding control nucleic acid molecule not contacted with the compound, indicates that the candidate compound modulates **ABC1** expression;

(2) a substantially pure nucleic acid (N1) comprising a region that is substantially identical to at least fifty contiguous nucleotides of nucleotides 5854 to 6694, 7756 to 8318, 10479 to 10825, 15214 to 16068, 21636 to 22111, 27898 to 28721, 32951 to 33743, 36065 to 36847, 39730 to 40577, 4543 to 5287, or 45081 to 55639 of the 183999 nucleotide sequence (I) defined in the specification;

(3) a substantially pure nucleic acid comprising a region that is substantially identical to nucleotides 1 to 28707 or 29011 to 53228 of (I);

(4) a cell expressing N1;

(5) a non-**human** mammal expressing N1;

(6) a method (M3) of treating a **human** having a higher than normal triglyceride level, comprising administering an **ABC1** polypeptide, or its triglyceride-regulating fragment, or a nucleic acid encoding the **ABC1** polypeptide or its triglyceride-regulating fragment;

(7) a non-**human** mammal comprising a transgene comprising a nucleic acid encoding a dominant-negative **ABC1** polypeptide, the dominant-negative polypeptide comprising a M1091T mutation;

(8) a method for determining whether a candidate compound decreases the **inhibition** of a dominant-negative **ABC1** polypeptide, the dominant-negative polypeptide comprising a M1091T mutation;

(9) a method for predicting a person's response to a triglyceride-lowering drug, comprising determining whether the person has a polymorphism in an **ABC1** gene, promoter, or regulatory sequence that alters the person's response to the drug;

(10) a method (M4) for determining whether a candidate compound is useful for modulating triglyceride levels;

(11) a method (M5) of determining a propensity for a disease or condition in a subject, where the disease or condition is selected from a lower than normal HDL level, a higher than normal triglyceride level, and a cardiovascular disease;

(12) a method (M6) for determining whether an **ABC1** polymorphism is indicative of a risk for a disease or condition in a subject, where the disease or condition is selected from lower than normal HDL level, a higher than normal triglyceride level, and a cardiovascular disease;

(13) an electronic database comprising sequence records of **ABC1** polymorphisms correlated to records of predisposition to or prevalence of a disease or condition selected from a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease;

(14) a method (M7) for selecting a preferred therapy for modulating **ABC1** activity or expression in a subject;

(15) a method (M8) for determining whether a candidate compound is useful for the treatment of a disease or condition selected from a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease;

(16) a method (M9) for identifying a compound to be tested for an ability to ameliorate or treat a disease or condition selected from a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease

(17) a method (M10) for determining whether a candidate compound is useful for modulating a disease or condition selected from a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease;

(18) a compound (C1) useful for the treatment of a disease or condition selected a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease;

(19) a compound that modulates **ABC1** activity and **binds** or interacts with an amino acid of **ABC1**, where the amino acid is a residue selected from amino acids 119 to 319 or 299 to 499 of **ABC1**;

(20) a method (M11) for determining whether a candidate compound is useful for modulating **ABC1** biological activity;

(21) a method (M12) for identifying a compound to be tested for an ability to modulate **ABC1** biological activity; and

(22) a method (M13) for screening a candidate LXR modulating compound for the ability to treat a disease or condition selected from a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

ACTIVITY - Cardiant; Antilipemic.

No biological data given.

MECHANISM OF ACTION - LXR- or RXR-mediated transcriptional activity modulator; ABC1 expression or activity modulator.

No biological data given.

USE - The LXR gene product may be used in an assay to identify compounds useful for the treatment of a disease or condition selected a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. Compounds that modulates the activity or expression of an LXR gene product are useful for treating a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease (all claimed).

The ABC1 polypeptide or its triglyceride-regulating fragment, or a nucleic acid encoding the ABC1 polypeptide or its triglyceride-regulating fragment are useful for treating humans having a higher than normal triglyceride level. The ABC1 polypeptide agonists/upregulators may be useful in the treatment of other diseases such as Alzheimer's disease, Niemann-Pick disease and Huntington's disease.

Dwg.0/27

L5 ANSWER 4 OF 101 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-182953 [18] WPIDS
DOC. NO. NON-CPI: N2001-130564
DOC. NO. CPI: C2001-054634
TITLE: Selecting agents that modulate ABCA transporters, useful e.g. for normalizing serum cholesterol levels, comprises using transgenic animals with an inactive ABCA gene allele.
DERWENT CLASS: B04 D16 P14 S03
INVENTOR(S): CHIMINI, G
PATENT ASSIGNEE(S): (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (CNRS) CNRS CENT NAT RECH SCI
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001009314	A1	20010208	(200118)*	FR	112

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2796808 A1 20010202 (200118)
AU 2000023000 A 20010219 (200129)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001009314	A1	WO 2000-FR209	20000128
FR 2796808	A1	FR 1999-9926	19990730
AU 2000023000	A	AU 2000-23000	20000128

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000023000	A	Based on	WO 200109314

PRIORITY APPLN. INFO: FR 1999-9926 19990730
AN 2001-182953 [18] WPIDS
AB WO 200109314 A UPAB: 20010402
NOVELTY - Selecting or screening agents (A) that modulate ABCA transporters (I), comprises using:
(i) non-**human** recombinant mammals with an inactivated allele of the gene (II) encoding (I); or
(ii) cells with an inactivated allele of (II), from any tissue of (i), preferably with an allele truncated in one or both exons corresponding to the first and/or second ATP-**binding** cassettes (NBD1 or 2).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method of selection or screening for (A);
(2) a homologous recombination vector containing an inactivated (preferably truncated) mammalian (II);
(3) use of a mammalian (I) expression vector, containing either the wild-type (II) or a (II) mutated in NBD1 or 2, for transformation of eukaryotic cells;
(4) expression vectors for (I) comprising an origin of replication functional in eukaryotes, a gene for selection of transformed cells, appropriate regulatory sequences and a sequence encoding (I), wild-type or mutated as in (3);
(5) eukaryotic host cells transformed with the vector of (4);
(6) production of non-**human**, recombinant mammals in which an allele of (II) is inactivated in NBD1;
(7) kits for assessing (A);
(8) (II) having:
(i) any of the sequences of 5762 base pairs (S1), 14044 bp (S2), 6607 bp (S32), or 23024 bp (S33), given in the specification; or
(ii) sequences 95% identical with (i);
(9) a mutated (I) having a point mutation in an ATP-**binding** cassette, especially in the Walker A motif;
(10) a reagent for detecting (I)-specific nucleotide sequences containing 15-50 nucleotides and able to amplify fragments encoding (I)-specific sequences, given in the specification; and
(11) a non-**human** recombinant mammal in which an allele of (I) is inactivated.
ACTIVITY - Antihypercholesterol. No suitable biological data is given.
MECHANISM OF ACTION - ABCA transporter.
USE - (A) that stimulate (I) may be useful for increasing (normalizing) serum levels of high-density lipoprotein cholesterol.
Dwg.0/24

L5 ANSWER 5 OF 101 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001287599 MEDLINE
DOCUMENT NUMBER: 21192304 PubMed ID: 11279031
TITLE: The zinc finger protein 202 (ZNF202) is a transcriptional repressor of ATP **binding** cassette transporter A1 (**ABCA1**) and ABCG1 gene expression and a modulator of cellular lipid efflux.
AUTHOR: Porsch-Ozcurumez M; Langmann T; Heimerl S; Borsukova H; Kaminski W E; Drobnik W; Honer C; Schumacher C; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry, University of Regensburg, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Apr 13) 276 (15) 12427-33.

Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered PubMed: 20010411
Entered Medline: 20010524

AB The zinc finger gene 202 (ZNF202) located within a hypoalphalipoproteinemia susceptibility locus on chromosome 11q23 is a transcriptional repressor of various genes involved in lipid metabolism. To provide further evidence for a functional linkage between ZNF202 and hypoalphalipoproteinemia, we investigated the effect of ZNF202 expression on ATP **binding** cassette transporter A1 (**ABCA1**) and ABCG1. **ABCA1** is a key regulator of the plasma high density lipoprotein pool size, whereas ABCG1 is another mediator of cellular cholesterol and phospholipid efflux in **human** macrophage. We demonstrate here that the full-length ZNF202m1 isoform **binds** to GnT repeats within the promotors of **ABCA1** (-229/-210) and ABCG1 (-572/-552). ZNF202m1 expression in HepG2 cells dose-dependently repressed the promotor activities of **ABCA1** and ABCG1. This transcriptional effect required the presence of the SCAN domain in ZNF202 and the functional integrity of a TATA box at position -24 of **ABCA1**, whereas the presence of GnT **binding** motifs was nonessential. The state of ZNF202 SCAN domain oligomerization affected the ability of the adjacent ZNF202 Kruppel-associated box domain to recruit the transcriptional corepressor KAP1. Overexpression of ZNF202m1 in RAW264.7 macrophages prevented the induction of **ABCA1** gene expression by 20(S)OH-cholesterol and 9-cis-retinoic acid, further substantiating the interference of ZNF202 in critical elements of transcriptional activation. Finally, HDL and apoAImediated lipid efflux was significantly reduced in RAW264.7 cells stably expressing ZNF202m1. In conclusion, we have identified **ABCA1** and ABCG1 as target genes for ZNF202-mediated repression and thus, provide evidence for a functional linkage between ZNF202 and hypoalphalipoproteinemia.

L5 ANSWER 6 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 2001:208874 BIOSIS
DOCUMENT NUMBER: PREV200100208874
TITLE: Specific docking of apolipoprotein A-I at the cell surface requires a functional **ABCA1** transporter.
AUTHOR(S): Chambenoit, Olivier; Hamon, Yannick; Marguet, Didier; Rigneault, Herve; Rosseneu, Maryvonne; Chimini, Giovanna (1)
CORPORATE SOURCE: (1) Centre d'Immunologie, INSERM-CNRS de Marseille Luminy, Parc Scientifique de Luminy, 13288, Marseille Cedex 09: chimini@ciml.univ-mrs.fr France
SOURCE: Journal of Biological Chemistry, (March 30, 2001) Vol. 276, No. 13, pp. 9955-9960. print.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The identification of defects in **ABCA1** as the molecular basis of Tangier disease has highlighted its crucial role in the loading with phospholipids and cholesterol of nascent apolipoprotein particles. Indeed the expression of **ABCA1** affects apolipoprotein A-I (apoA-I)-mediated removal of lipids from cell membranes, and the possible role of **ABCA1** as an apoA-I surface receptor has been recently suggested. In the present study, we have investigated the role of the **ABCA1** transporter as an apoA-I receptor with the analysis of a panel of transfectants expressing functional or mutant forms of **ABCA1**. We provide experimental evidence that the forced expression of a functional **ABCA1** transporter confers surface competence for apoA-I **binding**. This, however, appears to be dependent on **ABCA1** function. Structurally intact but ATPase-deficient forms of the transporter fail to elicit a specific cell association of the ligand. In addition the diffusion parameters of membrane-associated apoA-I indicate an interaction with membrane lipids rather than proteins. These results do not support a direct molecular interaction between **ABCA1** and apoA-I, but rather suggest that the **ABCA1** -induced modification of the lipid distribution in the membrane, evidenced by the phosphatidylserine exofacial flopping, generates a biophysical microenvironment required for the docking of apoA-I at the cell surface.

L5 ANSWER 7 OF 101 MEDLINE

ACCESSION NUMBER: 2001271827 MEDLINE

DOCUMENT NUMBER: 21221120 PubMed ID: 11309497
TITLE: A selective peroxisome proliferator-activated receptor delta agonist promotes reverse cholesterol transport.
AUTHOR: Oliver W R Jr; Shenk J L; Snaith M R; Russell C S; Plunket K D; Bodkin N L; Lewis M C; Winegar D A; Sznaidman M L; Lambert M H; Xu H E; Sternbach D D; Kliewer S A; Hansen B C; Willson T M
CORPORATE SOURCE: Metabolic Diseases Drug Discovery and Nuclear Receptor Discovery Research, GlaxoSmithKline, Research Triangle Park, NC 27709, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Apr 24) 98 (9) 5306-11.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered PubMed: 20010426
Entered Medline: 20010521

AB The peroxisome proliferator-activated receptors (PPARs) are dietary lipid sensors that regulate fatty acid and carbohydrate metabolism. The hypolipidemic effects of the fibrate drugs and the antidiabetic effects of the glitazone drugs in humans are due to activation of the alpha (NR1C1) and gamma (NR1C3) subtypes, respectively. By contrast, the therapeutic potential of the delta (NR1C2) subtype is unknown, due in part to the lack of selective ligands. We have used combinatorial chemistry and structure-based drug design to develop a potent and subtype-selective PPARdelta agonist, GW501516. In macrophages, fibroblasts, and intestinal cells, GW501516 increases expression of the reverse cholesterol transporter ATP-**binding** cassette A1 and induces apolipoprotein A1-specific cholesterol efflux. When dosed to insulin-resistant middle-aged obese rhesus monkeys, GW501516 causes a dramatic dose-dependent rise in serum high density lipoprotein cholesterol while lowering the levels of small-dense low density lipoprotein, fasting triglycerides, and fasting insulin. Our results suggest that PPARdelta agonists may be effective drugs to increase reverse cholesterol transport and decrease cardiovascular disease associated with the metabolic syndrome X.

L5 ANSWER 8 OF 101 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001200644 MEDLINE
DOCUMENT NUMBER: 21184766 PubMed ID: 11287605
TITLE: Identification of liver X receptor-retinoid X receptor as an activator of the sterol regulatory element-**binding** protein 1c gene promoter.
AUTHOR: Yoshikawa T; Shimano H; Amemiya-Kudo M; Yahagi N; Hasty A H; Matsuzaka T; Okazaki H; Tamura Y; Iizuka Y; Ohashi K; Osuga J; Harada K; Gotoda T; Kimura S; Ishibashi S; Yamada N
CORPORATE SOURCE: Department of Metabolic Diseases, University of Tokyo, Bunkyo-ku, Tokyo 113-8655, Japan.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (2001 May) 21 (9) 2991-3000.
Journal code: NGY; 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered PubMed: 20010405
Entered Medline: 20010517

AB In an attempt to identify transcription factors which activate sterol-regulatory element-**binding** protein 1c (SREBP-1c) transcription, we screened an expression cDNA library from adipose tissue of SREBP-1 knockout mice using a reporter gene containing the 2.6-kb mouse SREBP-1 gene promoter. We cloned and identified the oxysterol receptors liver X receptor (LXRalpha) and LXRbeta as strong activators of the mouse SREBP-1c promoter. In the transfection studies, expression of either LXRalpha or -beta activated the SREBP-1c promoter-luciferase gene in a dose-dependent manner. Deletion and mutation studies, as well as gel mobility shift assays, located an LXR response element complex consisting of two new LXR-**binding** motifs which showed high similarity to an LXR response element recently found in the **ABC1** gene promoter, a reverse cholesterol transporter. Addition of an LXR ligand,

22(R)-hydroxycholesterol, increased the promoter activity. Coexpression of retinoid X receptor (RXR), a heterodimeric partner, and its ligand 9-cis-retinoic acid also synergistically activated the SREBP-1c promoter. In HepG2 cells, SREBP-1c mRNA and precursor protein levels were induced by treatment with 22(R)-hydroxycholesterol and 9-cis-retinoic acid, confirming that endogenous LXR-RXR activation can induce endogenous SREBP-1c expression. The activation of SREBP-1c by LXR is associated with a slight increase in nuclear SREBP-1c, resulting in activation of the gene for fatty acid synthase, one of its downstream genes, as measured by the luciferase assay. These data demonstrate that LXR-RXR can modify the expression of genes for lipogenic enzymes by regulating SREBP-1c expression, providing a novel link between fatty acid and cholesterol metabolism.

L5 ANSWER 9 OF 101 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001265484 MEDLINE
DOCUMENT NUMBER: 21138379 PubMed ID: 11238261
TITLE: Common genetic variation in **ABCA1** is associated with altered lipoprotein levels and a modified risk for coronary artery disease.
AUTHOR: Clee S M; Zwinderman A H; Engert J C; Zwarts K Y; Molhuizen H O; Roomp K; Jukema J W; van Wijland M; van Dam M; Hudson T J; Brooks-Wilson A; Genest J Jr; Kastelein J J; Hayden M R
CORPORATE SOURCE: Centre for Molecular Medicine and Therapeutics, University of British Columbia, Vancouver, Canada.
SOURCE: CIRCULATION, (2001 Mar 6) 103 (9) 1198-205.
Journal code: DAW; 0147763. ISSN: 1524-4539.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered PubMed: 20010312
Entered Medline: 20010521
AB BACKGROUND: Low plasma HDL cholesterol (HDL-C) is associated with an increased risk of coronary artery disease (CAD). We recently identified the ATP-**binding** cassette transporter 1 (**ABCA1**) as the major gene underlying the HDL deficiency associated with reduced cholesterol efflux. Mutations within the **ABCA1** gene are associated with decreased HDL-C, increased triglycerides, and an increased risk of CAD. However, the extent to which common variation within this gene influences plasma lipid levels and CAD in the general population is unknown. METHODS AND RESULTS: We examined the phenotypic effects of single nucleotide polymorphisms in the coding region of **ABCA1**. The R219K variant has a carrier frequency of 46% in Europeans. Carriers have a reduced severity of CAD, decreased focal (minimum obstruction diameter 1.81+/-0.35 versus 1.73+/-0.35 mm in noncarriers, P:=0.001) and diffuse atherosclerosis (mean segment diameter 2.77+/-0.37 versus 2.70+/-0.37 mm, P:=0.005), and fewer coronary events (50% versus 59%, P:=0.02). Atherosclerosis progresses more slowly in carriers of R219K than in noncarriers. Carriers have decreased triglyceride levels (1.42+/-0.49 versus 1.84+/-0.77 mmol/L, P:=0.001) and a trend toward increased HDL-C (0.91+/-0.22 versus 0.88+/-0.20 mmol/L, P:=0.12). Other single nucleotide polymorphisms in the coding region had milder effects on plasma lipids and atherosclerosis. CONCLUSIONS: These data suggest that common variation in **ABCA1** significantly influences plasma lipid levels and the severity of CAD.

L5 ANSWER 10 OF 101 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001179473 EMBASE
TITLE: Novel polymorphisms in promoter region of ATP **binding** cassette transporter gene and plasma lipids, severity, progression, and regression of coronary atherosclerosis and response to therapy.
AUTHOR: Lutucuta S.; Ballantyne C.M.; Elghannam H.; Gotto A.M. Jr.; Marian A.J.
CORPORATE SOURCE: Dr. A.J. Marian, Section of Cardiology, One Baylor Plaza, Houston, TX 77030, United States. amarian@bcm.tmc.edu
SOURCE: Circulation Research, (11 May 2001) 88/9 (969-973).
Refs: 12
ISSN: 0009-7330 CODEN: CIRUAL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Identification of mutations in the ATP **binding** cassette transporter (**ABCA1**) gene in patients with Tangier disease, who exhibit reduced HDL cholesterol (HDL-C) and apolipoprotein A1 (apoA1) levels and premature coronary atherosclerosis, has led to the hypothesis that common polymorphisms in the **ABCA1** gene could determine HDL-C and apoA1 levels and the risk of coronary atherosclerosis in the general population. We sequenced a 660-bp 5' fragment of the **ABCA1** gene in 24 subjects and identified 3 novel polymorphisms: -477C/T, -419A/C, and -320G/C. We developed assays, genotyped 372 participants in the prospective Lipoprotein Coronary Atherosclerosis Study (LCAS), and determined the association of the variants with fasting plasma lipids and indices of quantitative coronary angiograms obtained at baseline and 2.5 years after randomization to fluvastatin or placebo. Distribution of -477C/T and -320G/C genotypes were 127 CC, 171 CT, and 74 TT and 130 GG, 168 GC, and 75 CC, respectively, and were in complete linkage disequilibrium (P<0.0001). Data for -477C/T are presented. The -419A/C variant was uncommon (present in 1 of 63 subjects). Heterozygous subjects had a modest reduction in HDL-C (P=0.09) and apoA1 (P=0.05) levels and a lesser response of apoA1 to treatment with fluvastatin (P=0.04). The mean number of coronary lesions causing 30% to 75% diameter stenosis was greater in subjects with the TT genotype (3.1.+-.2.1) or CT genotype (2.9.+-.1.9) than in subjects with the CC genotype (2.2.+-.1.8) (P=0.002). Similarly, compared with subjects with the CC genotype, greater numbers of subjects with the TT or CT genotype had .gtoreq.1 coronary lesion (P=0.001). No association between the genotypes and progression of coronary atherosclerosis or clinical events was detected. We conclude that **ABCA1** genotypes are potential risk factors for coronary atherosclerosis in the general population.

L5 ANSWER 11 OF 101 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:337903 CAPLUS
TITLE: Expression of the ATP-**Binding** Cassette Transporter Gene ABCG1 (ABC8) in Tangier Disease
AUTHOR(S): Lorkowski, Stefan; Kratz, Mario; Wenner, Claudia; Schmidt, Roland; Weitkamp, Benedikt; Fobker, Manfred; Reinhardt, Jurgen; Rauterberg, Jurgen; Galinski, Erwin Arno; Cullen, Paul
CORPORATE SOURCE: Institute of Arteriosclerosis Research, University of Munster, Munster, Germany
SOURCE: Biochem. Biophys. Res. Commun. (2001), 283(4), 821-830
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several members of the ATP-**binding** cassette (ABC) transporter family are involved in cholesterol efflux from cells. A defect in one member, **ABCA1**, results in Tangier disease, a condition characterized by cholesterol accumulation in macrophages and virtual absence of mature circulating high-d. lipoproteins. Expression of a second member, ABCG1, is increased by cholesterol-loading in **human** macrophages. We now show that ABCG1, which we identified by differential display RT-PCR in foamy macrophages, is overexpressed in macrophages from patients with Tangier disease compared to control macrophages. On examn. by confocal laser scanning microscopy, ABCG1 was present in perinuclear structures within the cell. In addn., a combination of in situ hybridization and indirect immunofluorescence microscopy revealed that ABCG1 is expressed in foamy macrophages within the atherosclerotic plaque. These data indicate that not only **ABCA1** but also ABCG1 may play a role in the cholesterol metab. of macrophages in vitro and in the atherosclerotic plaque. (c) 2001 Academic Press.

L5 ANSWER 12 OF 101 MEDLINE
ACCESSION NUMBER: 2001179458 MEDLINE
DOCUMENT NUMBER: 21092682 PubMed ID: 11162594
TITLE: Apolipoprotein specificity for lipid efflux by the **human** ABCAI transporter.
AUTHOR: Remaley A T; Stonik J A; Demosky S J; Neufeld E B; Bocharov A V; Vishnyakova T G; Eggerman T L; Patterson A P; Duverger N J; Santamarina-Fojo S; Brewer H B Jr
CORPORATE SOURCE: National Heart, Lung and Blood Institute, Bethesda, Maryland 20982, USA.. aremaley@nih.gov
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Jan 26) 280 (3) 818-23.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010222
Entered Medline: 20010329

AB ABCAI, a member of the ATP **binding** cassette family, mediates the efflux of excess cellular lipid to HDL and is defective in Tangier disease. The apolipoprotein acceptor specificity for lipid efflux by ABCAI was examined in stably transfected Hela cells, expressing a **human** ABCAI-GFP fusion protein. ApoA-I and all of the other exchangeable apolipoproteins tested (apoA-II, apoA-IV, apoC-I, apoC-II, apoC-III, apoE) showed greater than a threefold increase in cholesterol and phospholipid efflux from ABCAI-GFP transfected cells compared to control cells. Expression of ABCAI in Hela cells also resulted in a marked increase in specific **binding** of both apoA-I (Kd = 0.60 microg/mL) and apoA-II (Kd = 0.58 microg/mL) to a common **binding** site. In summary, ABCAI-mediated cellular **binding** of apolipoproteins and lipid efflux is not specific for only apoA-I but can also occur with other apolipoproteins that contain multiple amphipathic helical domains.

L5 ANSWER 13 OF 101 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001306508 MEDLINE
DOCUMENT NUMBER: 21157003 PubMed ID: 11257261
TITLE: Common variants in the gene encoding ATP-**binding** cassette transporter 1 in men with low HDL cholesterol levels and coronary heart disease.
AUTHOR: Brousseau M E; Bodzioch M; Schaefer E J; Goldkamp A L; Kielar D; Probst M; Ordovas J M; Aslanidis C; Lackner K J; Bloomfield Rubins H; Collins D; Robins S J; Wilson P W; Schmitz G
CORPORATE SOURCE: The Lipid Metabolism Laboratory, JM-USDA Human Nutrition Research Center on Aging at Tufts, Boston, MA, USA.
CONTRACT NUMBER: R01 HL60935 (NHLBI)
SOURCE: ATHEROSCLEROSIS, (2001 Feb 15) 154 (3) 607-11.
Journal code: 95X; 0242543. ISSN: 0021-9150.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered PubMed: 20010321
Entered Medline: 20010531

AB HDL cholesterol (HDL-C) deficiency is the most common lipid abnormality observed in patients with premature coronary heart disease (CHD). Recently, our laboratory and others demonstrated that mutations in the ATP-**binding** cassette transporter 1 (**ABCA1**) gene are responsible for Tangier disease, a rare genetic disorder characterized by severely diminished plasma HDL-C concentrations and a predisposition for CHD. To address the question of whether common variants within the coding sequence of **ABCA1** may affect plasma HDL-C levels and CHD risk in the general population, we determined the frequencies of three common **ABCA1** variants (G596A, A2589G and G3456C) in men participating in the Veterans Affairs Cooperative HDL Cholesterol Intervention Trial (VA-HIT), a study designed to examine the benefits of HDL raising in men having low HDL-C (< or =40 mg/dl) and established CHD, as well as in CHD-free men from the Framingham Offspring Study (FOS). Allele frequencies (%) in VA-HIT were 31, 16, and 4 for the G596A, A2589G, and G3456C variants, respectively, versus 27, 12, and 2 in FOS (P<0.03). None of the variants were significantly associated with plasma HDL-C concentrations in either population; however, in VA-HIT, the G3456C variant was associated with a significantly increased risk for CHD end points, suggesting a role for this variant in the premature CHD observed in this population.

L5 ANSWER 14 OF 101 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001306507 MEDLINE
DOCUMENT NUMBER: 21157002 PubMed ID: 11257260
TITLE: A point mutation in **ABC1** gene in a patient with severe premature coronary heart disease and mild clinical phenotype of Tangier disease.
AUTHOR: Bertolini S; Pisciotta L; Seri M; Cusano R; Cantafora A; Calabresi L; Franceschini G; Ravazzolo R; Calandra S
CORPORATE SOURCE: Department of Internal Medicine, University of Genoa, Viale Benedetto XV no. 6, I-16132 Genoa, Italy.
SOURCE: ATHEROSCLEROSIS, (2001 Feb 15) 154 (3) 599-605.
Journal code: 95X; 0242543. ISSN: 0021-9150.

PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered PubMed: 20010321
Entered Medline: 20010531

AB The proband is a 50 year-old woman born from a consanguineous marriage. She has been suffering from angina pectoris since the age of 38 and underwent coronary bypass surgery for three-vessel disease at 48. The presence of low plasma levels of total cholesterol and high density lipoprotein (HDL) cholesterol (2.4 and 0.1 mmol/l) and apo AI (<15 mg/dl), associated with corneal lesions and a mild splenomegaly suggested the diagnosis of Tangier disease. However, none of the other features of Tangier disease, including hepatomegaly, anemia and peripheral neuropathy, were present. The analysis of the dinucleotide microsatellites located in chromosome 9q31 region demonstrated that the proband was homozygous for the alleles of D9S53, D9S1784 and D9S1832. The mother and son of the proband, both with low levels of HDL cholesterol, shared one of the proband's haplotypes, whereas neither of these haplotypes was present in the normolipidemic proband's sister. The sequence of ATP-**binding** cassette transporter 1 (**ABC1**-1) cDNA obtained by reverse transcription-PCR (RT-PCR) of total RNA isolated from cultured fibroblasts showed that the proband was homozygous for a C>T transition in exon 13, which caused a tryptophane for arginine substitution (R527W). This mutation was confirmed by direct sequencing of exon 13 amplified from genomic DNA. It can be easily screened, as the nucleotide change introduces a restriction site for the enzyme Afl III. R527W substitution occurs in a highly conserved region of the NH2 cytoplasmic domain of **ABC1** protein. R527W co-segregates with the low HDL phenotype in the family and was not found in 200 chromosomes from normolipidemic individuals.

L5 ANSWER 15 OF 101 MEDLINE
ACCESSION NUMBER: 2001306475 MEDLINE
DOCUMENT NUMBER: 21155105 PubMed ID: 11229879
TITLE: ABC transporters and cholesterol metabolism.
AUTHOR: Schmitz G; Kaminski W E
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, 93042 Regensburg, Germany.. gerd.schmitz@klinik.uni-regensburg.de
SOURCE: FRONTIERS IN BIOSCIENCE, (2001 Mar 1) 6 D505-14. Ref: 103
Journal code: CUE; 9702166. ISSN: 1093-4715.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered PubMed: 20010320
Entered Medline: 20010531

AB ATP-**binding** cassette (ABC) proteins form a group of highly conserved cellular transmembrane transporters. Studies over the past year have implicated ABC transporters in cellular lipid trafficking processes. This notion has recently been confirmed and extended by the finding that the ABC transporter **ABCA1** is a key regulator of high-density lipoprotein (HDL) metabolism and macrophage targeting to the RES or the vascular wall. Expression of a large number of ABC transporters in monocytes/macrophages and their regulation by cholesterol flux render these transporter molecules potentially critical players in chronic inflammatory diseases such as atherosclerosis.

L5 ANSWER 16 OF 101 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001087277 EMBASE
TITLE: Novel approaches to treating cardiovascular disease: Lessons from Tangier disease.
AUTHOR: Oram J.F.
CORPORATE SOURCE: J.F. Oram, Department of Medicine, University of Washington, Box 356426, Seattle, WA 98195-6426, United States. joram@u.washington.edu
SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/3 (427-438).
Refs: 76
ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Atherosclerotic cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in Western societies. Although cholesterol is a major CVD risk factor, therapeutic interventions to lower plasma cholesterol levels have had limited success in reducing coronary events. Thus, novel approaches are needed to reduce or eliminate CVD. A potential therapeutic target is a newly discovered ATP **binding** cassette transporter called **ABCA1**, a cell membrane protein that is the gateway for secretion of excess cholesterol from macrophages into the high density lipoprotein (HDL) metabolic pathway. Mutations in **ABCA1** cause Tangier disease, a severe HDL deficiency syndrome characterised by accumulation of cholesterol in tissue macrophages and prevalent atherosclerosis. Studies of Tangier disease heterozygotes revealed that the relative activity of **ABCA1** determines plasma HDL levels and susceptibility to CVD. Drugs that induce **ABCA1** in mice increase clearance of cholesterol from tissues and **inhibit** intestinal absorption of dietary cholesterol. Thus, **ABCA1**-stimulating drugs have the potential to both mobilise cholesterol from atherosclerotic lesions and eliminate cholesterol from the body. By reducing plaque formation and rupture independently of the atherogenic factors involved, these drugs would be powerful agents for treating CVD.

L5 ANSWER 17 OF 101 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001260198 MEDLINE
DOCUMENT NUMBER: 21155672 PubMed ID: 11231917
TITLE: Localization of **human** ATP-**binding** cassette transporter 1 (**ABC1**) in normal and atherosclerotic tissues.
AUTHOR: Lawn R M; Wade D P; Couse T L; Wilcox J N
CORPORATE SOURCE: Winship Cancer Institute, Division of Hematology/Oncology, Emory University School of Medicine, Atlanta, GA, USA.
CONTRACT NUMBER: HL-58000 (NHLBI)
SOURCE: ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (2001 Mar) 21 (3) 378-85.
Journal code: B89; 9505803. ISSN: 1524-4636.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered PubMed: 20010320
Entered Medline: 20010517
AB The present study examines the expression of ATP-**binding** cassette transporter 1 (**ABC1**) mRNA in normal and atherosclerotic tissues by using in situ hybridization in an effort to better understand the function of this cholesterol transport protein. Samples of normal baboon tissues as well as **human** normal and atherosclerotic aortas were hybridized with (35)S-labeled **ABC1** sense and antisense riboprobes. Widespread expression of **ABC1** was observed generally in tissues containing inflammatory cells and lymphocytes. Other noninflammatory cells that were also sites of **ABC1** synthesis included the ductal cells of the kidney medulla, Leydig cells in the testis, and glial cells in the baboon cerebellum. Although normal veins and arteries did not express **ABC1** mRNA, it was found to be upregulated in the setting of atherosclerosis, where widespread expression was found in macrophages within atherosclerotic lesions. These results are consistent with the proposed role of **ABC1** in cholesterol transport in inflammatory cells. The specific upregulation of **ABC1** mRNA in the setting of atherosclerosis probably reflects the response of leukocytes to cholesterol loading. However, the presence of **ABC1** in ductal cells of the kidney medulla and in the small intestine suggest a more general role for this protein in cholesterol transport in other cell types.

L5 ANSWER 18 OF 101 EMBASE
ACCESSION NUMBER: 2001133907 EMBASE
TITLE: Reverse cholesterol transport and future pharmacological approaches to the treatment of atherosclerosis.

AUTHOR: Krause B.R.; Auerbach B.J.
CORPORATE SOURCE: B.R. Krause, Dept. of Cardiovasc. Therapeutics, Pfizer Global Res. and Development, Ann Arbor, MI 48105, United States. brian.krause@pfizer.com
SOURCE: Current Opinion in Investigational Drugs, (2001) 2/3 (375-381).
Refs: 55
ISSN: 0967-8298 CODEN: CIDREE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The apparent protective effect of high density lipoprotein cholesterol (HDL) with respect to coronary heart disease (CHD) is generally thought to reside in its ability to transport cholesterol from peripheral cells to the liver for excretion from the body. Known as reverse cholesterol transport (RCT), this process involves many key steps and lipoprotein interconversions, and there is no consensus as to which step is most suitable for possible drug intervention. The membrane proteins, scavenger receptor class B, type 1 (SR-B1) and the **ATP-binding cassette 1** (**ABC1**), have been strongly implicated as being important in cholesterol efflux; the former as a bona fide receptor for HDL and the latter as a lipid transporter. Lecithin:cholesterol acyltransferase (LCAT) then esterifies the effluxed cholesterol to form cholesteryl esters (Step 2), which are then transferred to apoB-containing lipoproteins by cholesteryl ester transfer protein (CETP, Step 3). Despite the complexities and uncertainties, drugs should be developed which impact all of the above steps, and short-term endpoints need to be defined for a cautious, systematic approach to clinical evaluation.

L5 ANSWER 19 OF 101 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000419618 EMBASE
TITLE: Tangier disease and **ABCA1**.
AUTHOR: Oram J.F.
CORPORATE SOURCE: J.F. Oram, University of Washington, Division of Metabolism, Endocrinology and Nutrition, Box 356426, Seattle, WA 98195-6426, United States. joram@u.washington.edu
SOURCE: Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, (15 Dec 2000) 1529/1-3 (321-330).
Refs: 61
ISSN: 1388-1981 CODEN: BBMLFG
PUBLISHER IDENT.: S 1388-1981(00)00157-8
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
029 Clinical Biochemistry
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Tangier disease is an autosomal recessive genetic disorder characterized by a severe high-density lipoprotein (HDL) deficiency, sterol deposition in tissue macrophages, and prevalent atherosclerosis. Mutations in the ATP **binding** cassette transporter **ABCA1** cause Tangier disease and other familial HDL deficiencies. **ABCA1** controls a cellular pathway that secretes cholesterol and phospholipids to lipid-poor apolipoproteins. This implies that an inability of newly synthesized apolipoproteins to acquire cellular lipids by the **ABCA1** pathway leads to their rapid degradation and an over-accumulation of cholesterol in macrophages. Thus, **ABCA1** plays a critical role in modulating flux of tissue cholesterol and phospholipids into the reverse cholesterol transport pathway, making it an important therapeutic target for clearing excess cholesterol from macrophages and preventing atherosclerosis. Copyright (C) 2000 Elsevier Science B.V.

L5 ANSWER 20 OF 101 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2001195083 MEDLINE
DOCUMENT NUMBER: 21092814 PubMed ID: 11178988
TITLE: Complete coding sequence, promoter region, and genomic structure of the **human** ABCA2 gene and evidence for sterol-dependent regulation in macrophages.
AUTHOR: Kaminski W E; Piehler A; Pullmann K; Porsch-Ozcurumez M; Duong C; Bared G M; Buchler C; Schmitz G

CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, 93042, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Feb 16) 281 (1) 249-58.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF327657; GENBANK-AF327658; GENBANK-AF327659; GENBANK-AF327660; GENBANK-AF327661; GENBANK-AF327662; GENBANK-AF327663; GENBANK-AF327664; GENBANK-AF327665; GENBANK-AF327666; GENBANK-AF327667; GENBANK-AF327668; GENBANK-AF327669; GENBANK-AF327670; GENBANK-AF327671; GENBANK-AF327672; GENBANK-AF327673; GENBANK-AF327674; GENBANK-AF327675; GENBANK-AF327676; GENBANK-AF327677; GENBANK-AF327678; GENBANK-AF327679; GENBANK-AF327680; GENBANK-AF327681; GENBANK-AF327682; GENBANK-AF327683; GENBANK-AF327684; GENBANK-AF327685; GENBANK-AF327686; GENBANK-AF327687; GENBANK-AF327688; GENBANK-AF327689; GENBANK-AF327690; GENBANK-AF327691; GENBANK-AF327692; GENBANK-AF327693; GENBANK-AF327694; GENBANK-AF327695; GENBANK-AF327696; GENBANK-AF327697; GENBANK-AF327698; GENBANK-AF327699; GENBANK-AF327700; GENBANK-AF327701; GENBANK-AF327702; GENBANK-AF327703; GENBANK-AF327704; GENBANK-AF327705
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered PubMed: 20010222
Entered Medline: 20010405

AB Members of the **human** ABC transporter A subfamily have gained considerable attention based on the recent findings that **ABCA1** and ABCR (ABCA4) cause familial HDL-deficiency syndromes and distinct forms of hereditary retinopathies, respectively. Here we report the complete cDNA and the genomic organization of ABCA2, another member of the **human** ABC A transporter subfamily. The ABCA2 coding region is 7.3 kb in size and codes for a 2436 amino acid polypeptide that bears the typical features of a full-size ABC transporter. Among the known members of the ABC A subfamily ABCA2 shares highest homology with the cholesterol-responsive transporters **ABCA1** (50%) and the recently cloned ABCA7 (44%). The ABCA2 gene comprises 48 exons which are localized within a genomic region of only 21 kb. Analysis of the putative ABCA2 promoter sequence revealed potential **binding** sites for transcription factors that are involved in the differentiation of myeloid and neural cells. Gene expression analysis in **human** macrophages showed that ABCA2 mRNA is induced during cholesterol import indicating that ABCA2 is a cholesterol-responsive gene. Our results suggest a potential role for ABCA2 in macrophage lipid metabolism and neural development.

L5 ANSWER 21 OF 101 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2001258237 MEDLINE
DOCUMENT NUMBER: 21103579 PubMed ID: 11181755
TITLE: Cellular cholesterol efflux is modulated by phospholipid-derived signaling molecules in familial HDL deficiency/Tangier disease fibroblasts.
AUTHOR: Haidar B; Mott S; Boucher B; Lee C Y; Marcil M; Genest J Jr
CORPORATE SOURCE: Cardiovascular Genetics Laboratory, McGill University Health Center, Royal Victoria Hospital, Montreal, Quebec, Canada H3A 1A1.
SOURCE: JOURNAL OF LIPID RESEARCH, (2001 Feb) 42 (2) 249-57.
Journal code: IX3; 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered PubMed: 20010222
Entered Medline: 20010517

AB Familial HDL deficiency (FHD) is the heterozygous form of Tangier disease (TD). Mutations of the **ABCA1** gene cause FHD and TD. FHD/TD cells are unable to normally efflux cholesterol onto nascent HDL particles, which are rapidly catabolized. TD fibroblasts have an abnormal pattern of PLC and PLD activation following cell stimulation with HDL(3) or apolipoprotein A-I (apoA-I). We examined cellular cholesterol efflux in FHD and TD fibroblasts by phospholipid-derived-molecules, compared with

that of normal cells. We used the PKC agonist 1,2-dioctanoylglycerol (DOG) and phorbol myristate acetate (PMA) to activate PKC, calphostin C, and GO 6976, as **inhibitors** of PKC; phosphatidic acid (PA), which is the product of PLD, and lysophosphatidic acid (LPA), phosphatidylcholine, sphingomyelin, and beta-cyclodextrin to investigate their potential effect in modulating cellular cholesterol efflux in [(3)H]cholesterol-labeled and cholesterol-loaded fibroblasts. Phosphatidylcholine, sphingomyelin, and beta-cyclodextrin promoted cholesterol efflux in an identical fashion in control, FHD, or TD fibroblasts. In a dose-dependent fashion, DOG (0-200 microM) increased apoA-I-mediated cellular cholesterol efflux by 40% in controls, 71% in FHD, and 242% in TD cells. PMA similarly increased cholesterol efflux to a maximum of 256% in controls, 182% in FHD, and 191% in TD cells. This effect was **inhibited** by calphostin C. PA (100 microM) also increased cholesterol efflux by 25% in control, 44% in FHD, and 100% in TD cells. Conversely, LPA reduced cholesterol efflux in a dose-dependent fashion in control and FHD cells (-50%, 200 microM) but not in TD cells, where efflux was increased by 140%. Propranolol (100 microM) significantly increased cholesterol efflux at 24 h in all three cell lines. n-Butanol partially decreased the DOG-mediated increase in cholesterol efflux. The **inhibitory** effect of calphostin C on DOG-stimulated cholesterol efflux could be partially overcome by propranolol, suggesting that PA is a downstream mediator of PKC-stimulated cholesterol efflux.We conclude that PLC and PLD activities are required for apoA-I-mediated cellular cholesterol efflux, and modulating cellular PA concentration can correct, at least partially, the cholesterol efflux defect in FHD and TD.

L5 ANSWER 22 OF 101 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2001155108 MEDLINE
DOCUMENT NUMBER: 21092592 PubMed ID: 11162504
TITLE: Accumulation of RhoA, RhoB, RhoG, and Rac1 in fibroblasts from Tangier disease subjects suggests a regulatory role of Rho family proteins in cholesterol efflux.
AUTHOR: Utech M; Hobbel G; Rust S; Reinecke H; Assmann G; Walter M
CORPORATE SOURCE: Institut fur Klinische Chemie und Laboratoriumsmedizin, Universitat Munster, Albert-Schweitzer-Str. 33, 48149 Munster, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Jan 12) 280 (1) 229-36.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010222
Entered Medline: 20010322

AB Tangier disease (TD) is an inherited disorder of lipid metabolism characterized by very low high density lipoprotein (HDL) plasma levels, cellular cholesteryl ester accumulation and reduced cholesterol excretion in response to HDL apolipoproteins. Molecular defects in the ATP **binding** cassette transporter 1 (**ABCA1**) have recently been identified as the cause of TD. **ABCA1** plays a key role in the translocation of cholesterol across the plasma membrane, and defective **ABCA1** causes cholesterol storage in TD cells. However, the exact relationship of many of the biochemical and morphological abnormalities in TD to **ABCA1** is unknown. Since small GTP-**binding** proteins are important regulators of many cellular functions, we characterized these proteins in normal and TD fibroblasts using the [alpha-32P]GTP overlay technique and Western blotting of SDS and isoelectric focusing gels. Our results indicate that GTP-**binding** proteins of the Rho family (RhoA, RhoB, RhoG, Rac-1) are enriched in fibroblasts from TD patients. The accumulation of small G proteins may have potential implications for the TD phenotype and the regulation of cholesterol excretion in TD cells. Copyright 2001 Academic Press.

L5 ANSWER 23 OF 101 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001174850 EMBASE
TITLE: Subpopulations of high density lipoproteins in homozygous and heterozygous Tangier disease.
AUTHOR: Asztalos B.F.; Brousseau M.E.; McNamara J.R.; Horvath K.V.; Roheim P.S.; Schaefer E.J.
CORPORATE SOURCE: B.F. Asztalos, J. Mayer USDA Hum. Nutr. Res. Ctr., Division of Endocrinology, New England Medical Center, 711 Washington Street, Boston, MA 02111, United States. belaasztalos@yahoo.com
SOURCE: Atherosclerosis, (2001) 156/1 (217-225).

Refs: 39
ISSN: 0021-9150 CODEN: ATHSBL
PUBLISHER IDENT.: S 0021-9150(00)00643-2
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Tangier disease (TD) is characterized by severe high-density lipoproteins (HDL) deficiency, hypercatabolism of HDL constituents, impaired cellular cholesterol efflux, and mutations in the gene of **ATP-binding cassette 1** (ABC-1). In the present study, we determined plasma lipid and apolipoprotein levels, and HDL subpopulations, in 110 subjects from a large TD kindred in which the proband was homozygous for an A.fwdarw.C missense mutation at nucleotide 5338 of the ABC-1 transcript. In the proband HDL-C, apoA-I, and apoA-II concentrations were 2, 1, and 2 mg/dl, respectively, apoA-I was present only in pre.beta.(1), while apoA-II was found free of apoA-I in two distinct .alpha. mobility subpopulations with different sizes. The smaller size particles contained only apoA-II while the larger one contained apoA-II and apo(a). Relative to unaffected male relatives (n=30), male heterozygotes (n=21) had significant reductions (P<0.001) in plasma HDL-C (-45%), apoA-I (-34%), apoA-II (-59%), apoA-IV (-40%), Lp(a) (-62%), and apoB (-55%) concentrations, and a significant increase (P<0.05, +33%) in plasma apoC-III levels. Female heterozygotes (n=11) similarly had significant reductions (P<0.001) in the concentrations of plasma HDL-C (-42%), apoA-I (-27%), apoA-II (-52%), Lp(a) (-27%), and (P<0.01) apoA-IV (-28%), apoB (-13%), and a significant increase (P<0.05) in plasma apoE levels (+29%) as compared to unaffected female relatives (n=41). Large size HDL subpopulations, especially the two LpA-I particles: .alpha.(1) and pre.alpha.(1) were dramatically reduced in both male and female heterozygotes relative to their unaffected family members. Since apoA-II decreased more than apoA-I in both male and female heterozygotes, the ratios of apoA-I/apoA-II were significantly (P<0.01) increased. The prevalence of CHD was 60% higher in the 32 heterozygotes than in the 71 unaffected relatives even though the latter group was on average 7 years older. We conclude that TD homozygotes have only pre.beta.(1) apoA-I-containing HDL subpopulations, while heterozygotes have HDL that is selectively depleted in the large .alpha.(1), pre.alpha.(1), and .alpha.(2), pre.alpha.(2) subpopulations, resulting in HDL particles that are small in size, poor in cholesterol, but relatively enriched in apoA-I compared to those of their unaffected relatives. These abnormalities appear to result in a higher risk of CHD in heterozygotes than in unaffected controls. .COPYRGT. 2001 Elsevier Science Ireland Ltd.

L5 ANSWER 24 OF 101 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 2001166542 MEDLINE
DOCUMENT NUMBER: 21165442 PubMed ID: 11264984
TITLE: Structure, function and regulation of the **ABC1** gene product.
AUTHOR: Schmitz G; Langmann T
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, Germany.. sgerd.schmitz@klinik.uni-regensburg.de
SOURCE: CURRENT OPINION IN LIPIDOLOGY, (2001 Apr) 12 (2) 129-40.
Ref: 99
Journal code: B05; 9010000. ISSN: 0957-9672.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered PubMed: 20010326
Entered Medline: 20010531

AB The role of the ATP-**binding** cassette transporter 1 (**ABCA1**) in cellular lipid efflux and high density lipoprotein metabolism has been recently documented by mutations in genetic HDL deficiency syndromes such as classical Tangier disease. Analysis of **ABCA1** knockout mice and overexpression studies have established the importance of **ABCA1** as a major determinant of HDL cholesterol in plasma. These studies also indicate that **ABCA1** is critically involved in cellular trafficking of cholesterol and choline-phospholipids and in total body lipid homeostasis, such as intestinal cholesterol and fat-soluble vitamin absorption and in the

modulation of steroidogenesis. First insights into the upregulation of **ABCA1** gene expression by cellular cholesterol and cAMP have identified critical **ABCA1** promoter elements, which **bind** the transcription factors liver X receptor, retinoid X receptor, Sp1 and E-box proteins. The finding that a lipid sensitive subgroup of ABC transporters is able to translocate cholesterol and phospholipids supports the concept that in **ABCA1** deficiency, compensatory mechanisms possibly involving MDR1, MDR3 and MRP-family members could be active. This suggests that a network of ABC transporters involved in cellular lipid transport exists, which is under the tight control of energy pathways directly linked to high density lipoprotein metabolism and atherogenesis.

L5 ANSWER 25 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:255260 BIOSIS
DOCUMENT NUMBER: PREV200100255260
TITLE: The role of the ATP **binding** cassette transporter A1 in arteriosclerosis.
AUTHOR(S): von Eckardstein, A. (1); Engel, T. (1); Li, Z. (1); Uehara, Y. (1); Zhou, X. (1); Langer, C.; Assmann, G. (1)
CORPORATE SOURCE: (1) Institute of Arteriosclerosis Research, University of Muenster, Muenster Germany
SOURCE: Pfluegers Archiv European Journal of Physiology, (2001) Vol. 441, No. 6 Supplement, pp. R122. print.
Meeting Info.: Joint Congress of the Scandinavian and the German Physiological Societies Berlin, Germany March 10-13, 2001
ISSN: 0031-6768.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 26 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:176618 BIOSIS
DOCUMENT NUMBER: PREV200100176618
TITLE: Identification and expression of multidrug resistance-related ABC transporter genes in Candida krusei.
AUTHOR(S): Katiyar, S. K.; Edlind, T. D. (1)
CORPORATE SOURCE: (1) Department of Microbiology and Immunology, MCP Hahnemann University, 2900 Queen Lane, Philadelphia, PA, 19129: edlind@drexel.edu USA
SOURCE: Medical Mycology, (February, 2001) Vol. 39, No. 1, pp. 109-116. print.
ISSN: 1369-3786.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Infections with Candida krusei have increased in recent years as a consequence of its intrinsic resistance to fluconazole, an antifungal azole widely used in immunocompromised individuals to suppress infections due to azole-susceptible C. albicans. One established mechanism for azole resistance is drug efflux by ATP **binding** cassette (ABC) transporters. Since these transporters recognize structurally diverse drugs, their overexpression can lead to multidrug resistance (MDR). To identify C. krusei genes potentially involved in azole resistance, PCR was performed with primers corresponding to conserved sequences of MDR-related ABC transporters from other fungi. Two genes, **ABC1** and ABC2, were identified; Southern blots suggested that both have one or two related gene copies in the C. krusei genome. **ABC1** RNA was constitutively expressed at low levels in log phase cells while ABC2 RNA was undetectable. However, both genes were upregulated as cultures approached stationary phase, and this upregulation was correlated with decreased susceptibility to the lethal activity of the azole derivative miconazole. Furthermore, **ABC1** was upregulated following brief treatment of C. krusei with miconazole and clotrimazole (but not other azoles), and the unrelated compounds albendazole and cycloheximide. The latter two compounds antagonized fluconazole activity versus C. krusei, supporting a role for the **ABC1** transporter in azole efflux. Finally, miconazole-resistant mutants selected in vitro demonstrated increased constitutive expression of **ABC1**. Based on these expression data, genetic and functional characterization of the **ABC1** transporter to directly test its role in C. krusei azole resistance would appear to be warranted.

L5 ANSWER 27 OF 101 MEDLINE
ACCESSION NUMBER: 2000431552 MEDLINE
DOCUMENT NUMBER: 20426878 PubMed ID: 10991725
TITLE: Lipid research. Possible new way to lower cholesterol.
COMMENT: Comment on: Science. 2000 Sep 1;289(5484):1524-9
AUTHOR: Ferber D

SOURCE: SCIENCE, (2000 Sep 1) 289 (5484) 1446-7.
Journal code: UJ7; 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
Commentary
News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914

L5 ANSWER 28 OF 101 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 2000:991956 PROMT
TITLE: EUROPEAN PATENT DISCLOSURES.(Brief Article)
SOURCE: BIOWORLD Today, (10 Nov 2000) Vol. 11, No. 219.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1933
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB September 21 (WO)
THIS IS THE FULL TEXT: COPYRIGHT 2000 American Health Consultants, Inc.

Subscription: $1350.00 per year. Published daily (5 times a week).

L5 ANSWER 29 OF 101 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 11
ACCESSION NUMBER: 2000:911440 CAPLUS
DOCUMENT NUMBER: 134:81739
TITLE: Compositions and methods for increasing cholesterol efflux and raising HDL using **human** ATP **binding** cassette transporter protein **ABC1**
INVENTOR(S): Lawn, Richard M.; Wade, David; Garvin, Michael
PATENT ASSIGNEE(S): CV Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078972	A2	20001228	WO 2000-US16765	20000616

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-140264 P 19990618
US 1999-153872 P 19990914
US 1999-166573 P 19991119

AB The present invention relates to novel **human ABC1** polypeptides and nucleic acid mols. encoding the same. The invention also relates to recombinant vectors, host cells, and compns. comprising **ABC1** polynucleotides, as well as to methods for producing **ABC1** polypeptides. The invention also relates to antibodies that **bind** specifically to **ABC1** polypeptides. In addn., the invention relates to methods for increasing cholesterol efflux as well as to methods for increasing **ABC1** expression and activity. The present invention further relates to methods for identifying compds. that modulate the expression of **ABC1** and methods for detecting the comparative level of **ABC1** polypeptides and polynucleotides in a mammalian subject. The present invention also provides kits and compns. suitable for screening compds. to det. the **ABC1** expression modulating activity of the compd., as well as kits and compns. suitable to det. whether a compd. modulates **ABC1**-dependent cholesterol efflux.

L5 ANSWER 30 OF 101 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 12
ACCESSION NUMBER: 2000:666871 CAPLUS
DOCUMENT NUMBER: 133:262303
TITLE: **Human ABC1** transporter and DNA and

methods for modulating cholesterol levels and diagnosing disease
INVENTOR(S): Hayden, Michael R.; Wilson, Angela R.; Pimstone, Simon N.
PATENT ASSIGNEE(S): University of British Columbia, Can.; Xenon Bioresearch, Inc.
SOURCE: PCT Int. Appl., 229 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055318	A2	20000921	WO 2000-IB532	20000315
WO 2000055318	A3	20010322		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1100895	A2	20010523	EP 2000-917240	20000315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
US 1999-124702 P 19990315
US 1999-138048 P 19990608
US 1999-139600 P 19990617
US 1999-151977 P 19990901
WO 2000-IB532 W 20000315

AB The invention features **ABC1** nucleic acids and proteins for the diagnosis and treatment of abnormal cholesterol regulation. The invention also features methods for identifying compds. for modulating cholesterol levels in an animal (e.g., a **human**). Thus, ABC transporter gene **ABC1** of chromosome 9 has been identified as the gene involved in Tangier disease and familial HDL deficiency. Many polymorphisms, and mutations (deletion, substitution, nonsense, frameshift, and splicing-altering), have been identified. Many of these correlate with disease; some create/delete restriction sites. The cDNA for **ABC1** has been cloned and sequenced. The protein encoded by the cDNA has an addnl. 60 amino acids relative to that previously reported: these extra amino acids were shown to be present in vivo and to play an essential part in the activity of the protein. The **ABC1** protein has been shown to transport cholesterol. The **ABC1** gene was found to have 49 exons. The sequence of each exon with surrounding introns is presented.

L5 ANSWER 31 OF 101 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:911439 CAPLUS
DOCUMENT NUMBER: 134:67162
TITLE: Compositions and methods for increasing cholesterol efflux and raising HDL using ATP **binding** cassette transporter protein **ABC1**
INVENTOR(S): Lawn, Richard M.; Wade, David; Oram, John F.; Garvin, Michael
PATENT ASSIGNEE(S): CV Therapeutics, Inc., USA; University of Washington
SOURCE: PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078971	A2	20001228	WO 2000-US16591	20000616
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
US 1999-140264 P 19990618

US 1999-153872 P 19990914
US 1999-166573 P 19991119

AB The present invention relates to novel **ABC1** polypeptides and nucleic acid mols. encoding the same. The invention also relates to recombinant vectors, host cells, and compns. comprising **ABC1** polynucleotides, as well as to methods for producing **ABC1** polypeptides. The invention also relates to antibodies that **bind** specifically to **ABC1** polypeptides. In addn., the invention relates to methods for increasing cholesterol efflux as well as to methods for increasing **ABC1** expression and activity. The present invention further relates to methods for identifying compds. that modulate the expression of **ABC1** and methods for detecting the comparative level of **ABC1** polypeptides and polynucleotides in a mammalian subject. The present invention also provides kits and compns. suitable for screening compds. to det. the **ABC1** expression modulating activity of the compd., as well as kits and compns. suitable to det. whether a compd. modulates **ABC1**-dependent cholesterol efflux.

L5 ANSWER 32 OF 101 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:227775 CAPLUS
DOCUMENT NUMBER: 132:275181
TITLE: ATP-**binding** cassette genes and proteins for diagnosis and treatment of lipid disorders and inflammatory diseases
INVENTOR(S): Schmitz, Gerd; Klucken, Jochen
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018912	A2	20000406	WO 1999-EP6991	19990921
WO 2000018912	A3	20000817		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9959804	A1	20000417	AU 1999-59804	19990921

PRIORITY APPLN. INFO.: US 1998-101706 P 19980925
WO 1999-EP6991 W 19990921

AB Cholesterol-responsive genes are identified by the differential display method in **human** monocytes from peripheral blood that were subjected to macrophage differentiation and cholesterol loading with acetylated LDL and subsequent deloading with HLD3. In an initial screen ABCGA (ABC8), a member of the rapidly growing family of ABC (ATP-**binding** cassette) transport systems that couple the energy of ATP hydrolysis to the translocation of solutes across biol. membranes, was identified as a cholesterol-sensitive switch. ABCG1 is upregulated by M-CSF-dependent phagocytic differentiation but expression is massively induced by cholesterol loading and almost completely set back to differentiation-dependent levels by HDL3. In a more detailed anal., 18 already characterized ABC members and 2 Fragment sequences were analyzed in monocyte/macrophage cells by RT-PCR as cholesterol sensitive. The most sensitive gene was ABCG1, which is the **human** homolog of the Drosophila white gene. Sequencing of the promoter of ABCG1 shows important transcription factor-**binding** sites relevant for phagocytic differentiation and lipid sensitivity. Antisense treatment of macrophages during cholesterol loading and HDL3-mediated deloading clearly identified ABCG1 as a cholesterol transporter. Among the other cholesterol-sensitive genes, **ABCA1** (**ABC1**) was further characterized, and identified in the mouse as an interleukin-1.beta. transporter involved also in apoptotic cell processing. Modulation of the activity of transmembrane proteins belonging to the ATP **binding** cassette transporter protein family which are etiol. involved in cholesterol-riven atherogenic processes and inflammatory diseases like psoriasis, lupus erythematodes and others provides therapeutic means to treat such diseases. Furthermore, detection of herein identified ABC transporter proteins of their resp. biochem. activities involved in such atherogenic and inflammatory processes provides diagnostic means for clin. application of diagnosis and monitoring of dyslipidemias, atherosclerosis

or inflammatory diseases like psoriasis and lupus erythematodes.

L5 ANSWER 33 OF 101 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-431298 [37] WPIDS
DOC. NO. NON-CPI: N2000-321863
DOC. NO. CPI: C2000-131075
TITLE: New non-**human** mammal comprising a non-functional endogenous ligand activated transcription factor-alpha allele, useful for screening retinoid X receptor agonists which reduce cholesterol levels or **inhibit** cholesterol absorption in mammals.
DERWENT CLASS: B04 D16 P14
INVENTOR(S): DIETSCHY, J M; MANGELSDORF, D J; REPA, J J; TURLEY, S D
PATENT ASSIGNEE(S): (TEXA) UNIV TEXAS SYSTEM
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000034461	A2	20000615	(200037)*	EN	117

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000020516 A 20000626 (200045)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000034461	A2	WO 1999-US29497	19991210
AU 2000020516	A	AU 2000-20516	19991210

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000020516	A Based on	WO 200034461

PRIORITY APPLN. INFO: US 1998-111894 19981210
AN 2000-431298 [37] WPIDS
AB WO 200034461 A UPAB: 20000807
NOVELTY - A non-**human** mammal (I) or a transgenic cell (II) comprising a non-functional endogenous LXR (ligand activated transcription factor) alpha allele, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method for screening (M1) a RXR (retinoid X receptor) agonist or LXR- alpha (ligand activated transcription factor) agonist candidate substance for increasing bile acid synthesis comprising contacting a cell with the candidate substance and then monitoring a bile acid phenotype of the cell;
(2) a method for screening (M2) a rexinoid for the ability to **inhibit** cholesterol absorption by an intestinal cell comprising treating the intestinal cell with a rexinoid and monitoring cholesterol absorption by the cell;
(3) a rexinoid compound (III) that **inhibits** cholesterol absorption identified by M2;
(4) a rexinoid compound that **inhibits** cholesterol absorption produced by a process comprising treating an intestinal cell with the rexinoid and then monitoring cholesterol absorption by the cell;
(5) a method for screening (M3) for a modulator of **ABC1** (ATP-**binding** cassette) expression comprising contacting a cell expressing an RXR with the candidate substance and determining the expression of **ABC1** expression in the cell; and
(6) making a modulator of **ABC1** expression comprising contacting a cell expressing an RXR with the candidate substance and determining the expression of **ABC1** expression in the cell.
ACTIVITY - Antilipemic; antiarteriosclerotic; cardiant.
MECHANISM OF ACTION - Cholesterol absorption **inhibitor**; bile acid synthesis enhancer; RXR/LXR alpha hormone receptor stimulator. The cholesterol absorption **inhibitory** activity of the RXR agonists was tested using LXR alpha wild type mice and knockout mice strains. Male, A129 strain mice (LXR alpha +/+ and -/-) were fed Teklad 7001 powdered diet supplemented with 0.2% cholesterol, 0.015% LG268 (a RXR-specific ligand) providing 30 mg/kg body weight for 10 days. On day 7, mice received a gavage dose of (22,23-3H)b-sitostanol and

(4-14C)cholesterol for the measurement of cholesterol absorption by the fecal isotope ratio method Turley et al., 1994. Cholesterol absorption was completely **inhibited** in mice receiving a dose of 30 mg/kg body weight over 10 days, regardless of LXR alpha genotype.

USE - (I) is used for screening a candidate substance for its ability to reduce cholesterol levels in a mammal which involves treating (I) with a candidate substance and then monitoring a cholesterol-related phenotype such as cholesterol absorption, circulating cholesterol, hepatic cholesterol, hepatomegaly atherosclerosis, cardiac failure, cardiac (atrophy/hypertropy), activity level, survival, cancer, reproduction, immune function, skin disease, cognitive function, and adrenal function, in the mammal. (I) is also used for screening a candidate substance for its ability to increase bile acid synthesis in a mammal. (III), a RXR agonist is used for reducing cholesterol levels or **inhibiting** cholesterol absorption in a mammal. The method further comprises treating a mammal, preferably humans with an agent that **inhibits** cholesterol biosynthesis such as HMG (high mobility group protein) CoA (coenzyme A) reductase **inhibitor**. The treatment also involves stimulating bile acid synthesis or reducing cholesterol intake (claimed). This method is thus useful for treating familial lipoprotein lipase deficiency and familial apolipoprotein C-II deficiency (autosomal recessive disorders), familial hypertriglyceridemia (an autosomal dominant disorder), familial defective apolipoprotein B-100, and familial combined hyperlipidemia. The transgenic animals serve as models for studying the effects of ligands specific for the RXR nuclear hormone receptor in transgenic LXR alpha knockout animal models.

ADVANTAGE - Cholesterol levels are lowered without any adverse side effects and LDL (low density lipoprotein) cholesterol levels are lowered without affecting total lipid levels.

Dwg.0/10

L5 ANSWER 34 OF 101 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-350569 [30] WPIDS
DOC. NO. CPI: C2000-106608
TITLE: Novel method of modulating amyloid deposition, used to treat amyloidosis, Alzheimer's disease, stroke or head injury, by administering adenosine triphosphate-**binding** cassette transporter or flippase blockers.
DERWENT CLASS: B05
INVENTOR(S): LAM, F C; REINER, P B
PATENT ASSIGNEE(S): (UYBR-N) UNIV BRITISH COLUMBIA
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000024390	A1	20000504	(200030)*	EN	86

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000011128 A 20000515 (200039)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000024390	A1	WO 1999-US23885	19991014
AU 2000011128	A	AU 2000-11128	19991014

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000011128	A Based on	WO 200024390

PRIORITY APPLN. INFO: US 1998-177413 19981023

AN 2000-350569 [30] WPIDS

AB WO 200024390 A UPAB: 20000624

NOVELTY - Modulating amyloid deposition in subjects comprising administering to the subjects an effective amount of at least one transporter blocker for an adenosine triphosphate (ATP)-**binding** cassette (ABC) transporter, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) packaged pharmaceutical compositions for treating amyloidosis

comprising a container holding an effective amount of a pharmaceutical composition for modulating amyloid deposition and instructions for using the composition for the treatment of amyloidosis;

(2) identifying agents that modulate amyloid deposition in organisms;

(3) identifying agents that modulate transport of amyloid- beta protein (A beta) across cellular membranes;

(4) modulating amyloid deposition in subjects by administering at least one blocker of flippase activity for an ABC transporter; and

(5) identifying agents that modulate flipping of amyloid across a cellular membrane.

ACTIVITY - Antiamyloidosis; nootropic; neuroprotective; cerebroprotective; antidiabetic.

MECHANISM OF ACTION - ABC transporter blocker; flippase blocker.

Various concentrations of RU-486 were used to treat GsrasDN1 PC12 cells to final concentrations of 3-3,000 nM of RU-486. Results indicated that increased APPs secretion in GsrasDN1 PC12 cells was RU-486 dose-dependent, with half-maximal effect at about 0.5 micro M. Concentration effect studies above 3.0 micro M RU-486 became difficult because RU-486 did not remain as a homogenous aqueous solution above that concentration. However, even at sub-maximal concentrations of RU-486, increased APPs secretion was noted (21-fold at 3 micro M RU-486).

USE - The methods are used for modulating amyloid deposition in subjects, to prevent or **inhibit** amyloid deposition, modulate cleavage of amyloid precursor protein (APP), modulate proteolytic processing of APP, such that the production of A beta is decreased or of APPs ('Swedish' mutant APP) is increased, modulate the ABC transporter's ability to export A beta from a cell or **inhibit** export of A beta from a cell (claimed). They are used to block MDR1, MDR3, **ABC1**, ABC2, ABC3, ABC7, ABC8, MRP4, MRP5 or the **human** ABC transporters encoded by the ESTs 45597, 122234, 123147, 131042, 157481, 82763, 352188 or 422562 (claimed). They are used to antagonize transport through one or more ABC transporters expressed in the brain or the cerebral microvasculature (claimed). They are used to treat disease states associated with amyloidosis including amyloid deposition associated with Alzheimer's disease and to treat stroke and head injury (claimed) characterized by cognitive and neurological defects associated with extracellular cerebrovascular amyloid deposits as well as Down's syndrome, hereditary cerebral hemorrhage amyloidosis, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia, chronic hemodialysis, familial amyloid cardiomyopathy, adult onset diabetes, insulinoma, gelsolin, cystatin C, familial amyloidotic polyneuropathy, Scrapie, Creutzfeldt-Jacob disease, kuru, Gerstmann-Straussler-Scheinker syndrome and bovine spongiform encephalopathy, and to treat or prevent amyloidosis.

DESCRIPTION OF DRAWING(S) - Dose-dependent effects of RU-486 administration upon APPs release from PC12 cells.

Dwg.4/15

L5 ANSWER 35 OF 101 MEDLINE DUPLICATE 13

ACCESSION NUMBER: 2001031139 MEDLINE
DOCUMENT NUMBER: 20490748 PubMed ID: 10918065
TITLE: Specific **binding** of ApoA-I, enhanced cholesterol efflux, and altered plasma membrane morphology in cells expressing **ABC1**.
AUTHOR: Wang N; Silver D L; Costet P; Tall A R
CORPORATE SOURCE: Division of Molecular Medicine, Department of Medicine, Columbia University, New York, New York 10032, USA.. nw30@columbia.edu
CONTRACT NUMBER: HL22682 (NHLBI)
HL56984 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Oct 20) 275 (42) 33053-8.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001120

AB Mutations of the **ABC1** transporter have been identified as the defect in Tangier disease, characterized by low HDL and cholesterol ester accumulation in macrophages. A full-length mouse **ABC1** cDNA was used to investigate the mechanisms of lipid efflux to apoA-I or HDL in transfected 293 cells. **ABC1** expression markedly increased cellular cholesterol and phospholipid efflux to apoA-I but had only minor effects on lipid efflux to HDL. The increased lipid efflux appears to involve a direct interaction between apoA-I and **ABC1**, because

ABC1 expression substantially increased apoA-I **binding** at the cell surface, and chemical cross-linking and immunoprecipitation analysis showed that apoA-I **binds** directly to **ABC1**. In contrast to scavenger receptor BI (SR-BI), another cell surface molecule capable of facilitating cholesterol efflux, **ABC1** preferentially bound lipid-free apoA-I but not HDL. Immunofluorescence confocal microscopy showed that **ABC1** is primarily localized on the cell surface. In the absence of apoA-I, cells overexpressing **ABC1** displayed a distinctive morphology, characterized by plasma membrane protrusions and resembling echinocytes that form when there are excess lipids in the outer membrane hemileaflet. The studies provide evidence for a direct interaction between **ABC1** and apoA-I, but not HDL, indicating that free apoA-I is the metabolic substrate for **ABC1**. Plasma membrane **ABC1** may act as a phospholipid/cholesterol flippase, providing lipid to bound apoA-I, or to the outer membrane hemileaflet.

L5 ANSWER 36 OF 101 MEDLINE
ACCESSION NUMBER: 2001023911 MEDLINE
DOCUMENT NUMBER: 20469425 PubMed ID: 10896940
TITLE: Scavenger receptor-BI **inhibits** ATP-**binding** cassette transporter 1- mediated cholesterol efflux in macrophages.
AUTHOR: Chen W; Silver D L; Smith J D; Tall A R
CORPORATE SOURCE: Division of Molecular Medicine, Department of Medicine, Columbia University, New York, New York 10032, USA.
CONTRACT NUMBER: HL 22682 (NHLBI)
HL 56984 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Oct 6) 275 (40) 30794-800.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20001023
Entered Medline: 20001113

AB Scavenger receptor BI (SR-BI) facilitates the efflux of cellular cholesterol to plasma high density lipoprotein (HDL). Recently, the ATP-**binding** cassette transporter 1 (**ABC1**) was identified as a key mediator of cholesterol efflux to apolipoproteins and HDL. The goal of the present study was to determine a possible interaction between the SR-BI and **ABC1** cholesterol efflux pathways in macrophages. Free cholesterol efflux to HDL was increased (approximately 2.2-fold) in SR-BI transfected RAW macrophages in association with increased SR-BI protein levels. Treatment of macrophages with 8-bromo-cAMP (cAMP) resulted in a 4.1-fold increase in **ABC1** mRNA level and also increased cholesterol efflux to HDL (2.2-fold) and apoA-I (5.5-fold). However, in SR-BI transfected RAW cells, cAMP treatment produced a much smaller increment in cholesterol efflux to HDL (1.1-fold) or apoA-I (3.3-fold) compared with control cells. In macrophages loaded with cholesterol by acetyl-LDL treatment, SR-BI overexpression did not increase cholesterol efflux to HDL but did **inhibit** cAMP-mediated cholesterol efflux to apoA-I or HDL. SR-BI neutralizing antibody led to a dose- and time-dependent increase of cAMP-mediated cholesterol efflux in both SR-BI transfected and control cells, indicating that SR-BI **inhibits** **ABC1**-mediated cholesterol efflux even at low SR-BI expression level. Transfection of a murine **ABC1** cDNA into 293 cells led to a 2.3-fold increase of cholesterol efflux to apoA-I, whereas co-transfection of SR-BI with **ABC1** blocked this increase in cholesterol efflux. SR-BI and **ABC1** appear to have distinct and competing roles in mediating cholesterol flux between HDL and macrophages. In nonpolarized cells, SR-BI promotes the reuptake of cholesterol actively effluxed by **ABC1**, creating a futile cycle.

L5 ANSWER 37 OF 101 MEDLINE
ACCESSION NUMBER: 2000496110 MEDLINE
DOCUMENT NUMBER: 20435820 PubMed ID: 10893411
TITLE: The correlation of **ATP-binding** **cassette 1** mRNA levels with cholesterol efflux from various cell lines.
AUTHOR: Bortnick A E; Rothblat G H; Stoudt G; Hoppe K L; Royer L J; McNeish J; Francone O L
CORPORATE SOURCE: MCP Hahnemann University, Department of Biochemistry, Philadelphia, Pennsylvania 19129, USA.
CONTRACT NUMBER: HL07443 (NHLBI)

HL22633 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Sep 15) 275 (37) 28634-40.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001013

AB Studies show that lipid-free apoA-I stimulates release of cholesterol and phospholipid from fibroblasts and macrophages. **ATP-binding cassette 1** (**ABC1**) is implicated in this release and has been identified as the genetic defect in Tangier disease, evidence that **ABC1** is critical to the biogenesis of high density lipoprotein. We quantified levels of **ABC1** mRNA, protein, and cholesterol efflux from J774 mouse macrophages +/- exposure to a cAMP analog. Up-regulating **ABC1** mRNA correlated to increased cholesterol efflux in a dose- and time-dependent manner. mRNA levels rose after 15 min of exposure while protein levels rose after 1 h, with increased efflux 2-4 h post-treatment. In contrast to cells from wild-type mice, peritoneal macrophages from the **Abc1** -/- mouse showed a lower level of basal efflux and no increase with cAMP treatment. The stimulation of efflux exhibits specificity for apoA-I, high density lipoprotein, and other apolipoproteins as cholesterol acceptors, but not for small unilamellar vesicles, bile acid micelles, or cyclodextrin. We have studied a number of cell types and found that while other cell lines express **ABC1** constitutively, only J774 and elicited mouse macrophages show a substantial increase of mRNA and efflux with cAMP treatment. ApoA-I-stimulated efflux was detected from the majority of cell lines examined, independent of treatment.

L5 ANSWER 38 OF 101 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 2000496057 MEDLINE
DOCUMENT NUMBER: 20428744 PubMed ID: 10858438
TITLE: Sterol-dependent transactivation of the **ABC1** promoter by the liver X receptor/retinoid X receptor.
AUTHOR: Costet P; Luo Y; Wang N; Tall A R
CORPORATE SOURCE: Division of Molecular Medicine, Department of Medicine, Columbia University, New York, New York 10032, USA.
CONTRACT NUMBER: HL54591 (NHLBI)
HL56984 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Sep 8) 275 (36) 28240-5.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001013

AB Tangier disease, a condition characterized by low levels of high density lipoprotein and cholesterol accumulation in macrophages, is caused by mutations in the ATP-**binding** cassette transporter **ABC1** . In cultured macrophages, **ABC1** mRNA was induced in an additive fashion by 22(R)-hydroxycholesterol and 9-cis-retinoic acid (9CRA), suggesting induction by nuclear hormone receptors of the liver X receptor (LXR) and retinoid X receptor (RXR) family. We cloned the 5'-end of the **human ABC1** transcript from cholesterol-loaded THP1 macrophages. When transfected into RAW macrophages, the upstream promoter was induced 7-fold by 22(R)-hydroxycholesterol, 8-fold by 9CRA, and 37-fold by 9CRA and 22(R)-hydroxycholesterol. Furthermore, promoter activity was increased in a sterol-responsive fashion when cotransfected with LXRalpha/RXR or LXRbeta/RXR. Further experiments identified a direct repeat spaced by four nucleotides (from -70 to -55 base pairs) as a **binding** site for LXRalpha/RXR or LXRbeta/RXR. Mutations in this element abolished the sterol-mediated activation of the promoter. The results show sterol-dependent transactivation of the **ABC1** promoter by LXR/RXR and suggest that small molecule agonists of LXR could be useful drugs to reverse foam cell formation and atherogenesis.

L5 ANSWER 39 OF 101 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 2001039011 MEDLINE
DOCUMENT NUMBER: 20504469 PubMed ID: 11035776

TITLE: Control of cellular cholesterol efflux by the nuclear oxysterol receptor LXR alpha.
AUTHOR: Venkateswaran A; Laffitte B A; Joseph S B; Mak P A; Wilpitz D C; Edwards P A; Tontonoz P
CORPORATE SOURCE: Department of Biological Chemistry, University of California, Los Angeles, CA 90095, USA.
CONTRACT NUMBER: HL 30568 (NHLBI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Oct 24) 97 (22) 12097-102. Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001128

AB LXR alpha is a nuclear receptor that has previously been shown to regulate the metabolic conversion of cholesterol to bile acids. Here we define a role for this transcription factor in the control of cellular cholesterol efflux. We demonstrate that retroviral expression of LXR alpha in NIH 3T3 fibroblasts or RAW264.7 macrophages and/or treatment of these cells with oxysterol ligands of LXR results in 7- to 30-fold induction of the mRNA encoding the putative cholesterol/phospholipid transporter ATP-**binding** cassette (ABC)A1. In contrast, induction of **ABCA1** mRNA in response to oxysterols is attenuated in cells that constitutively express dominant-negative forms of LXR alpha or LXR beta that lack the AF2 transcriptional activation domain. We further demonstrate that expression of LXR alpha in NIH 3T3 fibroblasts and/or treatment of these cells with oxysterols is sufficient to stimulate cholesterol efflux to extracellular apolipoprotein AI. The ability of oxysterol ligands of LXR to stimulate efflux is dramatically reduced in Tangier fibroblasts, which carry a loss of function mutation in the **ABCA1** gene. Taken together, these results indicate that cellular cholesterol efflux is controlled, at least in part, at the level of transcription by a nuclear receptor-signaling pathway. They suggest a model in which activation of LXRs by oxysterols in response to cellular sterol loading leads to induction of the **ABCA1** transporter and the stimulation of lipid efflux to extracellular acceptors. These findings have important implications for our understanding of mammalian cholesterol homeostasis and suggest new opportunities for pharmacological regulation of cellular lipid metabolism.

L5 ANSWER 40 OF 101 MEDLINE
ACCESSION NUMBER: 2000448573 MEDLINE
DOCUMENT NUMBER: 20455776 PubMed ID: 10998247
TITLE: Characterization of apolipoprotein-mediated HDL generation induced by cAMP in a murine macrophage cell line.
AUTHOR: Abe-Dohmae S; Suzuki S; Wada Y; Aburatani H; Vance D E; Yokoyama S
CORPORATE SOURCE: Biochemistry 1, Nagoya City University Medical School, Nagoya 467-8601, Japan.
SOURCE: BIOCHEMISTRY, (2000 Sep 12) 39 (36) 11092-9. Journal code: A0G; 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001013

AB Murine macrophage RAW264 were investigated for their response to lipid-free apolipoproteins. Preincubation of the cells with 300 microM dibutyryl cyclic (dBc) AMP for 16 h induced specific **binding** of apolipoprotein (apo) A-I to the cells and apoA-I-mediated HDL formation with cellular lipids, neither of which was detected in the absence of dBcAMP. Dose-dependent changes of the apoA-I specific **binding** and the apoA-I-mediated cholesterol release were largely superimposable. ApoA-II also mediated lipid release after the treatment of the cells with dBcAMP and effectively displaced the apoA-I **binding** to the cells. In contrast, cellular cholesterol efflux to lipid microemulsion and to 2-(hydroxypropyl)-beta-cyclodextrin was uninfluenced by the dBcAMP treatment. To induce the cellular reactivity with apoA-I, the incubation with dBcAMP required at least 6 h. Actinomycin D, cycloheximide, puromycin, and brefeldin A suppressed both the induction of apoA-I-mediated lipid release and the apoA-I specific **binding** to the cells. Analysis of the expression level of **ABC1** mRNA by using reverse transcription-polymerase chain reaction and oligonucleotide

arrays revealed that **ABC1** mRNA was already expressed in the dBcAMP-untreated cells, and the dBcAMP treatment for 16 h enhanced its expression 9-13-fold. We conclude that dBcAMP selectively induces apolipoprotein-mediated cellular lipid release and accordingly high-density lipoprotein generation by inducing specific **binding** of apolipoprotein, but does not influence diffusion-mediated lipid efflux. The cell-apolipoprotein interaction seems to depend on cellular protein biosynthesis and transport. A substantial increase in the level of **ABC1** mRNA caused by the dBcAMP treatment indicates that ATP-**binding** cassette transporter 1, the protein product of **ABC1**, may directly be responsible for the interaction, but the question about the absence of the interaction with its baseline expression level remains.

L5 ANSWER 41 OF 101 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 2000389202 MEDLINE
DOCUMENT NUMBER: 20345099 PubMed ID: 10884428
TITLE: Complete genomic sequence of the **human** **ABCA1** gene: analysis of the **human** and mouse ATP-**binding** cassette A promoter.
AUTHOR: Santamarina-Fojo S; Peterson K; Knapper C; Qiu Y; Freeman L; Cheng J F; Osorio J; Remaley A; Yang X P; Haudenschild C; Prades C; Chimini G; Blackmon E; Francois T; Duverger N; Rubin E M; Rosier M; Denefle P; Fredrickson D S; Brewer H B Jr
CORPORATE SOURCE: National Heart, Lung, and Blood Institute, and Clinical Center, Clinical Pathology Department, National Institutes of Health, Bethesda, MD 20892, USA..
silvia@mdb.nhlbi.nih.gov
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Jul 5) 97 (14) 7987-92.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF275948; GENBANK-AJ017356
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810

AB The **ABCA1** gene, a member of the ATP-**binding** cassette A (**ABCA1**) transporter superfamily, encodes a membrane protein that facilitates the cellular efflux of cholesterol and phospholipids. Mutations in **ABCA1** lead to familial high density lipoprotein deficiency and Tangier disease. We report the complete **human** **ABCA1** gene sequence, including 1,453 bp of the promoter, 146,581 bp of introns and exons, and 1 kb of the 3' flanking region. The **ABCA1** gene spans 149 kb and comprises 50 exons. Sixty-two repetitive Alu sequences were identified in introns 1-49. The transcription start site is 315 bp upstream of a newly identified initiation methionine codon and encodes an ORF of 6,783 bp. Thus, the **ABCA1** protein is comprised of 2,261 aa. Analysis of the 1,453 bp 5' upstream of the transcriptional start site reveals multiple **binding** sites for transcription factors with roles in lipid metabolism. Comparative analysis of the mouse and **human** **ABCA1** promoter sequences identified specific regulatory elements, which are evolutionarily conserved. The **human ABCA1** promoter fragment -200 to -80 bp that contains **binding** motifs for SP1, SP3, E-box, and AP1 modulates cellular cholesterol and cAMP regulation of **ABCA1** gene expression. These combined findings provide insights into **ABCA1**-mediated regulation of cellular cholesterol metabolism and will facilitate the identification of new pharmacologic agents for the treatment of atherosclerosis in humans.

L5 ANSWER 42 OF 101 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 2000226089 MEDLINE
DOCUMENT NUMBER: 20226089 PubMed ID: 10760292
TITLE: High density lipoprotein deficiency and foam cell accumulation in mice with targeted disruption of ATP-**binding** cassette transporter-1.
AUTHOR: McNeish J; Aiello R J; Guyot D; Turi T; Gabel C; Aldinger C; Hoppe K L; Roach M L; Royer L J; de Wet J; Broccardo C; Chimini G; Francone O L
CORPORATE SOURCE: Central Research Division, Pfizer Incorporated, Eastern Point Road, Groton, CT 06340, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Apr 11) 97 (8) 4245-50.
Journal code: PV3; 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000517

AB Recently, the **human** ATP-**binding** cassette transporter-1 (**ABC1**) gene has been demonstrated to be mutated in patients with Tangier disease. To investigate the role of the **ABC1** protein in an experimental in vivo model, we used gene targeting in DBA-1J embryonic stem cells to produce an **ABC1**-deficient mouse. Expression of the murine **Abc1** gene was ablated by using a nonisogenic targeting construct that deletes six exons coding for the first nucleotide-**binding** fold. Lipid profiles from **Abc1** knockout (-/-) mice revealed an approximately 70% reduction in cholesterol, markedly reduced plasma phospholipids, and an almost complete lack of high density lipoproteins (HDL) when compared with wild-type littermates (+/+). Fractionation of lipoproteins by FPLC demonstrated dramatic alterations in HDL cholesterol (HDL-C), including the near absence of apolipoprotein AI. Low density lipoprotein (LDL) cholesterol (LDL-C) and apolipoprotein B were also significantly reduced in +/- and -/- compared with their littermate controls. The inactivation of the **Abc1** gene led to an increase in the absorption of cholesterol in mice fed a chow or a high-fat and -cholesterol diet. Histopathologic examination of **Abc1**-/- mice at ages 7, 12, and 18 mo demonstrated a striking accumulation of lipid-laden macrophages and type II pneumocytes in the lungs. Taken together, these findings demonstrate that **Abc1**-/- mice display pathophysiologic hallmarks similar to **human** Tangier disease and highlight the capacity of **ABC1** transporters to participate in the regulation of dietary cholesterol absorption.

L5 ANSWER 43 OF 101 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 2000409898 MEDLINE
DOCUMENT NUMBER: 20396633 PubMed ID: 10938021
TITLE: Common and rare **ABCA1** variants affecting plasma HDL cholesterol.
AUTHOR: Wang J; Burnett J R; Near S; Young K; Zinman B; Hanley A J; Connelly P W; Harris S B; Hegele R A
CORPORATE SOURCE: John P. Robarts Research Institute, London, Ontario, Canada.
CONTRACT NUMBER: 1-R21-DK44597-01 (NIDDK)
SOURCE: ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (2000 Aug) 20 (8) 1983-9.
Journal code: B89; 9505803. ISSN: 1079-5642.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000831

AB Mutations in **ABCA1**, a member of the ATP-**binding** cassette family, have been shown to underlie Tangier disease (TD) and familial hypoalphalipoproteinemia (FHA), which are genetic disorders that are characterized by depressed concentrations of plasma high density lipoprotein (HDL) cholesterol. An important question is whether common variants within the coding sequence of **ABCA1** can affect plasma HDL cholesterol in the general population. To address this issue, we developed a screening strategy to find common **ABCA1** variants. This strategy involved long-range amplification of genomic DNA by using coding sequences only, followed by deep sequencing into the introns. This method helped us to characterize a new set of amplification primers, which permitted amplification of virtually all of the coding sequence of **ABCA1** and its intron-exon boundaries with a single DNA amplification program. With these new sequencing primers, we found 3 novel **ABCA1** mutations: a frameshift mutation (4570insA, A1484S-->X1492), a missense mutation (A986D) in a TD family, and a missense mutation (R170C) in aboriginal subjects with FHA. We also used these sequencing primers to characterize 4 novel common amino acid variants in **ABCA1**, in addition to 5 novel common silent variants. We tested for association of the **ABCA1** I/M823 variant with plasma HDL cholesterol in Canadian Inuit and found that M823/M823 homozygotes had significantly higher plasma HDL cholesterol compared with subjects with the other genotypes. The results provide proof of principle of the effectiveness of this approach to identify both rare and common **ABCA1** genomic variants and also suggest that common amino acid

variation in **ABCA1** is a determinant of plasma HDL cholesterol in the general population.

L5 ANSWER 44 OF 101 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 2000473146 MEDLINE
DOCUMENT NUMBER: 20341799 PubMed ID: 10884295
TITLE: Cellular cholesterol efflux in heterozygotes for tangier disease is markedly reduced and correlates with high density lipoprotein cholesterol concentration and particle size.
AUTHOR: Brousseau M E; Eberhart G P; Dupuis J; Asztalos B F; Goldkamp A L; Schaefer E J; Freeman M W
CORPORATE SOURCE: Lipid Metabolism Laboratory, JM-USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA 02111, USA.
CONTRACT NUMBER: HL-09319 (NHLBI)
HL-45098 (NHLBI)
SOURCE: JOURNAL OF LIPID RESEARCH, (2000 Jul) 41 (7) 1125-35.
Journal code: IX3; 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001005

AB Tangier disease (TD), caused by mutations in the **ATP-binding cassette 1** (ABC-1) gene, is a rare genetic disorder characterized by severe deficiency of high density lipoproteins (HDL) in the plasma, hypercatabolism of HDL, and defective apolipoprotein (apo)-mediated cellular cholesterol efflux. In the present study, we assessed plasma lipid concentrations, HDL particle size and subspecies, and cellular cholesterol efflux in 9 TD heterozygotes from a kindred in which the proband was homozygous for an A-->C missense mutation at nucleotide 5338 of the ABC-1 transcript. Relative to age- and gender-matched controls from the Framingham Offspring Study (FOS), TD heterozygotes had significant reductions (P < 0.000) in HDL-C (-54% female; -40% male) and apoA-I (-33% female; -37% male) concentrations, as well as significantly less cholesterol (-68% female; -58% male) distributed in the largest HDL subclasses, H5 and H4. Consequently, HDL particle size (nm) was significantly smaller (P < 0.000) in TD heterozygotes (8.6 +/- 0.6 female; 8.7 +/- 0.1 male) relative to FOS controls (9.4 +/- 0.4 female; 9.0 +/- 0.3 male). Further studies demonstrated that apoA-I-mediated cellular cholesterol efflux in TD heterozygotes was essentially half that of controls (11 +/- 2 vs. 20 +/- 3% of total [(3)H]cholesterol, P < 0. 001), with strong correlations observed between cholesterol efflux and both HDL-C level (r = 0.600) and particle size (r = 0.680).In summary, our data demonstrate that apolipoprotein-mediated cholesterol efflux is aberrant in TD heterozygotes, as it is in homozygotes. This finding, along with the associations observed between HDL-C concentration, HDL particle size, and cholesterol efflux, supports the concept that plasma HDL-C levels are regulated, in part, by cholesterol efflux, which in turn influences HDL particle size and, ultimately, HDL apoA-I catabolism.

L5 ANSWER 45 OF 101 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 2000475411 MEDLINE
DOCUMENT NUMBER: 20437687 PubMed ID: 10980140
TITLE: Functional loss of **ABCA1** in mice causes severe placental malformation, aberrant lipid distribution, and kidney glomerulonephritis as well as high-density lipoprotein cholesterol deficiency.
AUTHOR: Christiansen-Weber T A; Voland J R; Wu Y; Ngo K; Roland B L; Nguyen S; Peterson P A; Fung-Leung W P
CORPORATE SOURCE: R. W. Johnson Pharmaceutical Research Institute, San Diego, California 92121, USA.
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (2000 Sep) 157 (3) 1017-29.
Journal code: 3RS; 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20000929

AB Tangier disease (TD) and familial HDL deficiency (FHA) have recently been linked to mutations in the **human** ATP-**binding** cassette

transporter 1 (hABCA1), a member of the ABC superfamily. Both diseases are characterized by the lowering or lack of high-density lipoprotein cholesterol (HDL-C) and low serum cholesterol. The murine **ABCA1** -/- phenotype corroborates the **human** TD linkage to **ABCA1** . Similar to TD in humans, HDL-C is virtually absent in **ABCA1**-/- mice accompanied by a reduction in serum cholesterol and lipid deposition in various tissues. In addition, the placenta of **ABCA1**-/- mice is malformed, resulting in severe embryo growth retardation, fetal loss, and neonatal death. The basis for these defects appears to be altered steroidogenesis, a direct result of the lack of HDL-C. By 6 months of age, **ABCA1**-/- animals develop membranoproliferative glomerulonephritis due to deposition of immunocomplexes followed by cardiomegaly with ventricular dilation and hypertrophy, ultimately succumbing to congestive heart failure. This murine model of TD will be very useful in the study of lipid metabolism, renal inflammation, and cardiovascular disease and may reveal previously unsuspected relationships between them.

L5 ANSWER 46 OF 101 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 2001086702 MEDLINE
DOCUMENT NUMBER: 20427713 PubMed ID: 10970803
TITLE: Cloning, characterization and tissue distribution of the rat ATP-**binding** cassette (ABC) transporter ABC2/ABCA2.
AUTHOR: Zhao L X; Zhou C J; Tanaka A; Nakata M; Hirabayashi T; Amachi T; Shioda S; Ueda K; Inagaki N
CORPORATE SOURCE: Department of Physiology, Akita University School of Medicine, 1-1-1, Hondo, Akita 010-8543, Japan.
SOURCE: BIOCHEMICAL JOURNAL, (2000 Sep 15) 350 Pt 3 865-72. Journal code: 9YO. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB037924; GENBANK-AB037937
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010102
Entered Medline: 20010118

AB The **ABC1** (ABCA) subfamily of the ATP-**binding** cassette (ABC) transporter superfamily has a structural feature that distinguishes it from other ABC transporters. Here we report the cloning, molecular characterization and tissue distribution of ABC2/ABCA2, which belongs to the **ABC1** subfamily. Rat ABC2 is a protein of 2434 amino acids that has 44.5%, 40.0% and 40.8% identity with mouse **ABC1**/**ABCA1**, **human** ABC3/ABCA3 and **human** ABCR/ABCA4 respectively. Immunoblot analysis showed that proteins of 260 and 250 kDa were detected in COS-1 cells transfected with ABC2 having a haemagglutinin tag, while no band was detected in mock-transfected cells. After incubation with N-glycosidase F, the mobilities of the two proteins increased and a single band was detected, suggesting that ABC2 is a glycoprotein. Photoaffinity labelling with 8-azido-[alpha-(32)P]ATP confirmed that ATP **binds** to the ABC2 protein in the presence of Mg(2+). RNA blot analysis showed that ABC2 mRNA is most abundant in rat brain. Examination of brain by in situ hybridization determined that ABC2 is expressed at high levels in the white matter, indicating that it is expressed in the oligodendrocytes. ABC2, therefore, is a glycosylated ABC transporter protein, and may play an especially important role in the brain. In addition, the N-terminal 60-amino-acid sequence of the **human ABC1**, which was missing from previous reports, has been determined.

L5 ANSWER 47 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:438477 BIOSIS
DOCUMENT NUMBER: PREV200000438477
TITLE: **ABC1** gene expression and ApoA-I-mediated cholesterol efflux are regulated by LXR.
AUTHOR(S): Schwartz, Karen; Lawn, Richard M.; Wade, David P. (1)
CORPORATE SOURCE: (1) CV Therapeutics Inc., 3172 Porter Drive, Palo Alto, CA, 94304 USA
SOURCE: Biochemical and Biophysical Research Communications, (August 11, 2000) Vol. 274, No. 3, pp. 794-802. print. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB ATP-**binding** cassette transporter 1 (**ABC1**) mediates the active efflux of cholesterol from cells to apolipoproteins. To study the mechanisms of regulation of **ABC1** gene expression, RAW 264.7

macrophages were transiently transfected with **ABC1** promoter-luciferase reporter gene-fusion constructs. Transcription from a 1.64 kb fragment was induced by cholesterol loading but was not responsive to cAMP. Treatment of the cells with 9-cis retinoic acid or 20(S)-hydroxycholesterol, ligands for the nuclear receptors LXR and RXR, resulted in a marked induction of luciferase expression. The responsible control element was mapped to an imperfect direct repeat of the nuclear receptor half-site TGACCT separated by four bases (DR-4) that **binds** LXR/RXR heterodimers. Endogenous **ABC1** gene expression in RAW cells and apolipoprotein A-I mediated cholesterol efflux were also upregulated by both receptor ligands. These findings raise the possibility that ligands that activate the LXR-RXR heterodimer may be useful for the therapeutic modulation of the **ABC1** pathway.

L5 ANSWER 48 OF 101 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 2001155545 MEDLINE
DOCUMENT NUMBER: 21077322 PubMed ID: 11209972
TITLE: High-density lipoprotein: gene-based approaches to the prevention of atherosclerosis.
AUTHOR: Rong J X; Fisher E A
CORPORATE SOURCE: Department of Medicine, The Zena and Michael Wiener Cardiovascular Institute, Mount Sinai School of Medicine, New York, NY 10029, USA.
CONTRACT NUMBER: HL 61814 (NHLBI)
SOURCE: ANNALS OF MEDICINE, (2000 Dec) 32 (9) 642-51. Ref: 73
Journal code: AMD; 8906388. ISSN: 0785-3890.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010207
Entered Medline: 20010322

AB Although the atheroprotective role of high-density lipoprotein (HDL) has been well documented in epidemiological and animal studies, highly effective therapeutic approaches for the selective increase of plasma HDL levels or function are not yet available. Several mechanisms by which HDL exerts an atheroprotective effect have been proposed on the basis of experiments in vitro and in vivo. These mechanisms include directing excess cellular cholesterol from the peripheral tissues to the liver in 'reverse cholesterol transport', **inhibiting** oxidative modification or aggregation of LDL, and modulating inflammatory responses to favour vasoprotection. This review gives an overview of the genes regulating these mechanisms, such as those encoding apolipoprotein AI, lecithin:cholesterol acyltransferase (LCAT), scavenger receptor B1 (SR-BI), and the ATP-**binding** cassette transporter 1 (**ABC1**), and the potential to exploit them to develop gene-based therapeutic approaches to increase the level or function of HDL.

L5 ANSWER 49 OF 101 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 2000400462 MEDLINE
DOCUMENT NUMBER: 20334305 PubMed ID: 10873640
TITLE: Identification of a novel **human** sterol-sensitive ATP-**binding** cassette transporter (ABCA7).
AUTHOR: Kaminski W E; Orso E; Diederich W; Klucken J; Drobnik W; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Franz-Josef-Strauss-Allee 11, Regensburg, D-93042, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000 Jul 5) 273 (2) 532-8.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF250238
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000817

AB We report the identification of the full-length cDNA for a novel ATP-**binding** cassette (ABC) transporter from **human** macrophages. The mRNA is of 6.8 kb size and contains an open reading frame encoding a polypeptide of 2146 amino acids with a calculated molecular

weight of 220 kDa. The predicted protein product is composed of two transmembrane domains and two nucleotide **binding** folds indicating that it pertains to the group of full-size ABC transporters. The novel transporter shows highest protein sequence homology with the recently cloned **human** cholesterol and phospholipid exporter **ABCA1** (54%) and the **human** retinal transporter ABCR (49%), both members of the ABC transporter subfamily A. In accordance with the currently proposed classification, the novel transporter was designated ABCA7. ABCA7 mRNA was detected predominantly in myelo-lymphatic tissues with highest expression in peripheral leukocytes, thymus, spleen, and bone marrow. Expression of ABCA7 is induced during in vitro differentiation of **human** monocytes into macrophages. In macrophages, both the ABCA7 mRNA and protein expression are upregulated in the presence of modified low density lipoprotein and downregulated by HDL(3). Our results suggest a role for ABCA7 in macrophage transmembrane lipid transport.

L5 ANSWER 50 OF 101 MEDLINE
ACCESSION NUMBER: 2000501460 MEDLINE
DOCUMENT NUMBER: 20500387 PubMed ID: 11048892
TITLE: ABC transporters in cellular lipid trafficking.
AUTHOR: Schmitz G; Kaminski W E; Orso E
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Germany.. gerd.schmitz@klinik.uni-regensburg.de
SOURCE: CURRENT OPINION IN LIPIDOLOGY, (2000 Oct) 11 (5) 493-501. Ref: 75
Journal code: B05. ISSN: 0957-9672.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010213
Entered Medline: 20010215

AB ATP-**binding** cassette (ABC) transporters constitute a group of evolutionary highly conserved cellular transmembrane transport proteins. Recent work has implicated ABC transporters in cellular transmembrane lipid transport and hereditary diseases have been causatively linked to defective ABC transporters translocating lipid compounds. The emerging concept that a defined subset of ABC transporters is intimately involved in cellular lipid trafficking has recently been substantiated convincingly by the finding that **ABCA1** plays a central role in the regulation of HDL metabolism and macrophage targeting to the RES or the vascular wall. Differentiation dependent expression of a large number of ABC transporters in monocytes/macrophages and their regulation by sterol flux render these transporter molecules potentially critical players in atherogenesis and other chronic inflammatory diseases.

L5 ANSWER 51 OF 101 MEDLINE DUPLICATE 24
ACCESSION NUMBER: 2000261282 MEDLINE
DOCUMENT NUMBER: 20261282 PubMed ID: 10799318
TITLE: Analysis of hABC1 gene 5' end: additional peptide sequence, promoter region, and four polymorphisms.
AUTHOR: Pullinger C R; Hakamata H; Duchateau P N; Eng C; Aouizerat B E; Cho M H; Fielding C J; Kane J P
CORPORATE SOURCE: Department of Physiology, University of California, San Francisco, California, USA.. clivep@itsa.ucsf.edu
CONTRACT NUMBER: HL 07731 (NHLBI)
HL 31210 (NHLBI)
HL 57976 (NHLBI)
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000 May 10) 271 (2) 451-5.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000622
Last Updated on STN: 20000714
Entered Medline: 20000613

AB Evidence linking mutations in ATP-**binding**-cassette transporter gene 1 (**ABC1**) to Tangier disease suggests it functions in the

active transport of free cholesterol out of cells. Since its mRNA level is regulated in response to cellular cholesterol stores it is of interest to explore its promoter response elements, and to investigate polymorphisms for their contributions to the prevalence of low levels of HDL in the population that promotes premature coronary heart disease. Investigation of the 5' end of the gene by 5' RACE analysis revealed 455 nucleotides additional to published sequences, and predicts another 60 amino acid N-terminal residues, resulting in a 2261-residue protein. Protein sequence analysis predicts a membrane-spanning region and possible signal peptide. The 5' flanking region was located by a **Human** Research Project BLAST search. This region contains regulatory elements that potentially control **ABC1** gene expression. In addition to numerous SP1 **binding** sites there are four putative sterol regulatory elements (SREs). Our studies uncovered three single nucleotide substitution polymorphisms, one in the promoter region and two in the 5' untranslated region (5'UTR), plus an insertion/deletion polymorphism. Copyright 2000 Academic Press.

L5 ANSWER 52 OF 101 MEDLINE DUPLICATE 25
ACCESSION NUMBER: 2000171564 MEDLINE
DOCUMENT NUMBER: 20171564 PubMed ID: 10706591
TITLE: Novel mutations in the gene encoding **ATP-binding cassette 1** in four tangier disease kindreds.
AUTHOR: Brousseau M E; Schaefer E J; Dupuis J; Eustace B; Van Eerdewegh P; Goldkamp A L; Thurston L M; FitzGerald M G; Yasek-McKenna D; O'Neill G; Eberhart G P; Weiffenbach B; Ordovas J M; Freeman M W; Brown R H Jr; Gu J Z
CORPORATE SOURCE: Lipid Metabolism Laboratory, JM-USDA Human Nutrition Research Center on Aging at Tufts University and Department of Medicine, New England Medical Center, Boston, MA 02111, USA.
CONTRACT NUMBER: HL-09319 (NHLBI)
HL-45098 (NHLBI)
SOURCE: JOURNAL OF LIPID RESEARCH, (2000 Mar) 41 (3) 433-41.
Journal code: IX3; 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000509

AB Tangier disease (TD) is an autosomal co-dominant disorder in which homozygotes have a marked deficiency of high density lipoprotein (HDL) cholesterol and, in some cases, peripheral neuropathy and premature coronary heart disease (CHD). Homozygotes are further characterized by cholesteryl ester deposition in various tissues throughout the body, most notably in those of the reticuloendothelial system. Several studies have demonstrated that the excess lipid deposition in TD is due to defective apolipoprotein-mediated efflux of cellular cholesterol and phospholipids. Although much progress has been made in our understanding of the metabolic basis of TD, the precise molecular defect had remained elusive until very recently. By positional cloning methods, we: 1) confirm the assignment of TD to chromosome 9q31, 2) provide evidence that **human ATP-binding cassette-1** (hABC-1) maps to a 250 kb region on 9q31, and 3) describe novel deletion, insertion, and missense mutations in the gene encoding hABC-1 in four unrelated TD kindreds. These results establish a causal role for mutations in hABC-1 in TD and indicate that this transporter has a critical function in the regulation of intracellular lipid trafficking that dramatically affects plasma HDL cholesterol levels.

L5 ANSWER 53 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 26
ACCESSION NUMBER: 2001:1326 BIOSIS
DOCUMENT NUMBER: PREV200100001326
TITLE: Mutations in **ABC1** in Tangier disease and familial high-density lipoprotein deficiency.
AUTHOR(S): Marcil, Michel (1); Brooks-Wilson, Angie; Kastelein, John; Hayden, Michael; Genest, Jacques, Jr. (1)
CORPORATE SOURCE: (1) Laboratoire de genetique cardio-vasculaire, Institut de recherches cliniques de Montreal, 110, Avenue des Pins Ouest, Montreal, PQ, H2 1R7 Canada
SOURCE: M-S (Medecine Sciences), (March, 2000) Vol. 16, No. 3, pp. 421-423. print.
ISSN: 0767-0974.
DOCUMENT TYPE: Article
LANGUAGE: French

SUMMARY LANGUAGE: English

L5 ANSWER 54 OF 101 MEDLINE DUPLICATE 27
ACCESSION NUMBER: 2000435274 MEDLINE
DOCUMENT NUMBER: 20342793 PubMed ID: 10878804
TITLE: **ABC1** promotes engulfment of apoptotic cells and transbilayer redistribution of phosphatidylserine.
AUTHOR: Hamon Y; Broccardo C; Chambenoit O; Luciani M F; Toti F; Chaslin S; Freyssinet J M; Devaux P F; McNeish J; Marguet D; Chimini G
CORPORATE SOURCE: Centre d'Immunologie INSERM-CNRS de Marseille Luminy, Marseille, France.
SOURCE: NATURE CELL BIOLOGY, (2000 Jul) 2 (7) 399-406.
Journal code: DIQ; 100890575. ISSN: 1465-7392.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921
AB ATP-**binding**-cassette transporter 1 (**ABC1**) has been implicated in processes related to membrane-lipid turnover. Here, using in vivo loss-of-function and in vitro gain-of-function models, we show that **ABC1** promotes Ca2+-induced exposure of phosphatidylserine at the membrane, as determined by a prothrombinase assay, membrane microvesiculation and measurement of transbilayer redistribution of spin-labelled phospholipids. That **ABC1** promotes engulfment of dead cells is shown by the impaired ability of **ABC1**-deficient macrophages to engulf apoptotic preys and by the acquisition of phagocytic behaviour by **ABC1** transfectants. Release of membrane phospholipids and cholesterol to apo-AI, the protein core of the cholesterol-shuttling high-density lipoprotein (HDL) particle, is also **ABC1**-dependent. We propose that both the efficiency of apoptotic-cell engulfment and the efflux of cellular lipids depend on **ABC1**-induced perturbation of membrane phosphatidylserine turnover. Transient local exposure of anionic phospholipids in the outer membrane leaflet may be sufficient to alter the general properties of the membrane and thus influence discrete physiological functions.

L5 ANSWER 55 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:422245 BIOSIS
DOCUMENT NUMBER: PREV200000422245
TITLE: Acceleration of reverse cholesterol transport.
AUTHOR(S): von Eckardstein, Arnold (1); Nofer, Jerzy-Roch; Assmann, Gerd
CORPORATE SOURCE: (1) Zentrallaboratorium, Institut fuer Klinische Chemie und Laboratoriumsmedizin, Westfaelische Wilhelms-Universitaet Muenster, Albert-Schweitzer-Strasse 33, D-48129, Muenster Germany
SOURCE: Current Opinion in Cardiology, (September, 2000) Vol. 15, No. 5, pp. 348-354. print.
ISSN: 0268-4705.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 56 OF 101 MEDLINE DUPLICATE 28
ACCESSION NUMBER: 2001101433 MEDLINE
DOCUMENT NUMBER: 20563909 PubMed ID: 11111099
TITLE: Tangier disease and **ABCA1**.
AUTHOR: Oram J F
CORPORATE SOURCE: University of Washington, Division of Metabolism, Endocrinology and Nutrition, Box 356426, Seattle, WA 98195-6426, USA.. joram@u.washington.edu
CONTRACT NUMBER: DK02456 (NIDDK)
HL53451 (NHLBI)
HL55362 (NHLBI)
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (2000 Dec 15) 1529 (1-3) 321-30. Ref: 61
Journal code: AOW. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010124
Entered Medline: 20010201

AB Tangier disease is an autosomal recessive genetic disorder characterized by a severe high-density lipoprotein (HDL) deficiency, sterol deposition in tissue macrophages, and prevalent atherosclerosis. Mutations in the ATP **binding** cassette transporter **ABCA1** cause Tangier disease and other familial HDL deficiencies. **ABCA1** controls a cellular pathway that secretes cholesterol and phospholipids to lipid-poor apolipoproteins. This implies that an inability of newly synthesized apolipoproteins to acquire cellular lipids by the **ABCA1** pathway leads to their rapid degradation and an over-accumulation of cholesterol in macrophages. Thus, **ABCA1** plays a critical role in modulating flux of tissue cholesterol and phospholipids into the reverse cholesterol transport pathway, making it an important therapeutic target for clearing excess cholesterol from macrophages and preventing atherosclerosis.

L5 ANSWER 57 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:298960 BIOSIS
DOCUMENT NUMBER: PREV200000298960
TITLE: Inherited disorders of transport in the liver.
AUTHOR(S): Thompson, Richard; Strautnieks, Sandr
SOURCE: Current Opinion in Genetics & Development, (June, 2000) Vol. 10, No. 3, pp. 310-313. print.
ISSN: 0959-437X.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 58 OF 101 MEDLINE DUPLICATE 29
ACCESSION NUMBER: 2000481276 MEDLINE
DOCUMENT NUMBER: 20338188 PubMed ID: 10882340
TITLE: **ABCA1**-mediated transport of cellular cholesterol and phospholipids to HDL apolipoproteins.
AUTHOR: Oram J F; Vaughan A M
CORPORATE SOURCE: Department of Medicine, University of Washington, Seattle 98195, USA.. joram@u.washington.edu
CONTRACT NUMBER: DK02456 (NIDDK)
HL18645 (NHLBI)
HL55362 (NHLBI)
SOURCE: CURRENT OPINION IN LIPIDOLOGY, (2000 Jun) 11 (3) 253-60.
Ref: 56
Journal code: B05; 9010000. ISSN: 0957-9672.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001010

AB Lipid-poor apolipoproteins remove cellular cholesterol and phospholipids by an active transport pathway controlled by an ATP **binding** cassette transporter called **ABCA1** (formerly **ABC1**). Mutations in **ABCA1** cause Tangier disease, a severe HDL deficiency syndrome characterized by a rapid turnover of plasma apolipoprotein A-I, accumulation of sterol in tissue macrophages, and prevalent atherosclerosis. This implies that lipidation of apolipoprotein A-I by the **ABCA1** pathway is required for generating HDL particles and clearing sterol from macrophages. Thus, the **ABCA1** pathway has become an important therapeutic target for mobilizing excess cholesterol from tissue macrophages and protecting against atherosclerosis.

L5 ANSWER 59 OF 101 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 30
ACCESSION NUMBER: 2000:231580 CAPLUS
DOCUMENT NUMBER: 133:15022
TITLE: ATP-**binding** cassette transporter A1 (**ABCA1**) in macrophages: a dual function in inflammation and lipid metabolism?
AUTHOR(S): Schmitz, G.; Kaminski, W. E.; Porsch-Ozcurumez, M.; Klucken, J.; Orso, E.; Bodzioch, M.; Buchler, C.; Drobnik, W.
CORPORATE SOURCE: Institute of Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, D-93042, Germany

SOURCE: Pathobiology (2000), Volume Date 1999, 67(5-6), 236-240
CODEN: PATHEF; ISSN: 1015-2008
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activated lipid-laden macrophages in the vascular wall are key modulators of the inflammatory processes underlying atherosclerosis. We demonstrate here that the ATP-**binding** cassette (ABC) transporter **ABCA1** is induced during differentiation of **human** monocytes into macrophages. **ABCA1** has been implicated in macrophage interleukin-1.beta. secretion and apoptosis. Moreover, **ABCA1** mRNA and protein levels are strongly upregulated by uptake of modified LDL and downregulated by HDL3-mediated lipid efflux in macrophages. Mutation anal. in patients with the classical Tangier disease (TD), a monogenetic disorder characterized by hypersplenism, macrophage accumulation and deposition of cholesteryl esters in the reticuloendothelial system, low plasma HDL and premature atherosclerosis, revealed deleterious mutations in their **ABCA1** gene. The localization pattern of the mutations within the **ABCA1** protein appears to det. the tropism for either the reticuloendothelial system, as seen in the classical TD phenotype, or the artery wall, as in the case of HDL deficiency in the absence of splenomegaly. In a comprehensive anal. of the expression and regulation of all currently known **human** ABC transporters, we identified addnl. cholesterol-responsive genes that are induced during monocyte differentiation into macrophages. Our results indicate a dual regulatory function for **ABCA1** in macrophage lipid metab. and inflammation.

REFERENCE COUNT: 5
REFERENCE(S):
(1) Andrei, C; Mol Biol Cell 1999, V105, P1463
(2) Bodzioch, M; Nat Genet 1999, V22, P347 CAPLUS
(3) Hamon, Y; Blood 1997, V90, P2911 CAPLUS
(4) Klucken, J; Proc Natl Acad Sci USA in press
(5) Langmann, T; Biochem Biophys Res Commun 1999, V257/1, P29

L5 ANSWER 60 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:386524 BIOSIS
DOCUMENT NUMBER: PREV200000386524
TITLE: Apolipoprotein-mediated cellular cholesterol/phospholipid efflux and plasma high density lipoprotein level in mice.
AUTHOR(S): Tsujita, Maki; Tomimoto, Shigehiro; Okumura-Noji, Kuniko; Okazaki, Mitsuyo; Yokoyama, Shinji (1)
CORPORATE SOURCE: (1) Biochemistry 1, Nagoya City University Medical School, Mizuho-ku, Nagoya, 467-8601 Japan
SOURCE: Biochimica et Biophysica Acta, (31 May, 2000) Vol. 1485, No. 2-3, pp. 199-213. print.
ISSN: 0006-3002.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Helical apolipoprotein(apo)s generate pre-beta-high density lipoprotein (HDL) by removing cellular cholesterol and phospholipid upon the interaction with cells. To investigate its physiological relevance, we studied the effect of an in vitro **inhibitor** of this reaction, probucol, in mice on the cell-apo interaction and plasma HDL levels. Plasma HDL severely dropped in a few days with probucol-containing chow while low density protein decreased more mildly over a few weeks. The peritoneal macrophages were assayed for apoA-I **binding**, apoA-I-mediated release of cellular cholesterol and phospholipid and the reduction by apoA-I of the ACAT-available intracellular cholesterol pool. All of these parameters were strongly suppressed in the probucol-fed mice. In contrast, the mRNA levels of the potential regulatory proteins of the HDL level such as apoA-I, apoE, LCAT, PLTP, SRB1 and **ABC1** did not change with probucol. The fractional clearance rate of plasma HDL-cholesteryl ester was uninfluenced by probucol, but that of the HDL-apoprotein was slightly increased. No measurable CETP activity was detected either in the control or probucol-fed mice plasma. The change in these functional parameters is consistent with that observed in the Tangier disease patients. We thus concluded that generation of HDL by apo-cell interaction is a major source of plasma HDL in mice.

L5 ANSWER 61 OF 101 MEDLINE DUPLICATE 31
ACCESSION NUMBER: 2000120723 MEDLINE
DOCUMENT NUMBER: 20120723 PubMed ID: 10655069
TITLE: Transport of lipids from golgi to plasma membrane is defective in tangier disease patients and **Abc1** -deficient mice.
AUTHOR: Orso E; Broccardo C; Kaminski W E; Bottcher A; Liebisch G;

Drobnik W; Gotz A; Chambenoit O; Diederich W; Langmann T; Spruss T; Luciani M F; Rothe G; Lackner K J; Chimini G; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, Germany.
SOURCE: NATURE GENETICS, (2000 Feb) 24 (2) 192-6.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000228

AB Mutations in the gene encoding ATP-**binding** cassette transporter 1 (**ABC1**) have been reported in Tangier disease (TD), an autosomal recessive disorder that is characterized by almost complete absence of plasma high-density lipoprotein (HDL), deposition of cholesteryl esters in the reticulo-endothelial system (RES) and aberrant cellular lipid trafficking. We demonstrate here that mice with a targeted inactivation of **Abc1** display morphologic abnormalities and perturbations in their lipoprotein metabolism concordant with TD. **ABC1** is expressed on the plasma membrane and the Golgi complex, mediates apo-AI associated export of cholesterol and phospholipids from the cell, and is regulated by cholesterol flux. Structural and functional abnormalities in caveolar processing and the trans-Golgi secretory pathway of cells lacking functional **ABC1** indicate that lipid export processes involving vesicular budding between the Golgi and the plasma membrane are severely disturbed.

L5 ANSWER 62 OF 101 MEDLINE DUPLICATE 32
ACCESSION NUMBER: 2001065739 MEDLINE
DOCUMENT NUMBER: 20525454 PubMed ID: 11072082
TITLE: Genomic organization and characterization of the promoter of the **human** ATP-**binding** cassette transporter-G1 (ABCG1) gene.
AUTHOR: Langmann T; Porsch-Ozcurumez M; Unkelbach U; Klucken J; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Franz-Josef-Strauss-Allee 11, 93042, Regensburg, Germany.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (2000 Nov 15) 1494 (1-2) 175-80.
Journal code: A0W. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ289137; GENBANK-AJ289138; GENBANK-AJ289139; GENBANK-AJ289140; GENBANK-AJ289141; GENBANK-AJ289142; GENBANK-AJ289143; GENBANK-AJ289144; GENBANK-AJ289145; GENBANK-AJ289146; GENBANK-AJ289147; GENBANK-AJ289148; GENBANK-AJ289149; GENBANK-AJ289150; GENBANK-AJ289151
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20001214
Entered Medline: 20001222

AB The ATP-**binding** cassette transporter G1 (ABCG1) was recently identified as a regulator of macrophage cholesterol and phospholipid transport. This transporter together with **ABCA1** belongs to a group of sterol-sensitive ABC proteins which are induced by lipid loading or specific oxysterols. We report here the genomic structure of ABCG1 along with the 5' flanking sequence using library screening and BLAST search analysis. The ABCG1 gene spans more than 70 kb and contains 15 exons. The exon size is between 30 and 1081 bp and the introns range in size from 137 bp to more than 45 kb. All exon-intron boundaries display the canonical GT/AG sequences. Using promoter-luciferase reporter assays in the myeloid cell lines THP-1 and RAW246.7 and the hepatoma cell line HepG2 we could demonstrate the functionality of the ABCG1 promoter and the minimal sequence requirements for gene expression. The TATA-less proximal promoter contains multiple Sp1 **binding** sites and a consensus sequence for sterol regulatory element **binding** protein.

L5 ANSWER 63 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:275034 BIOSIS
DOCUMENT NUMBER: PREV200000275034

TITLE: Genes influencing HDL metabolism: New perspectives and implications for atherosclerosis prevention.
AUTHOR(S): Rader, Daniel J. (1); Maugeais, Cyrille
CORPORATE SOURCE: (1) Preventive Cardiology and Lipid Research Center, University of Pennsylvania Medical Center, 614 BRBII/III 421 Curie Blvd., Philadelphia, PA, 19104 USA
SOURCE: Molecular Medicine Today, (April, 2000) Vol. 6, No. 4, pp. 170-175. print..
ISSN: 1357-4310.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Atherosclerotic cardiovascular disease (ASCVD) is the most common cause of morbidity and mortality in Western societies. Current therapies, such as reduction of plasma cholesterol, significantly reduce, but do not come close to eliminating, the complications of ASCVD. Therefore, novel therapeutic approaches to the prevention of acute coronary events and progression of atherosclerosis are still needed. The complex metabolism of high density lipoproteins represents an attractive potential target for therapeutic intervention. Here, we will discuss those components of the high density lipoprotein metabolism and lipid transport pathways that are potential preventative or therapeutic targets for ASCVD.

L5 ANSWER 64 OF 101 MEDLINE
ACCESSION NUMBER: 2000256258 MEDLINE
DOCUMENT NUMBER: 20256258 PubMed ID: 10798400
TITLE: Molecular basis for K(ATP) assembly: transmembrane interactions mediate association of a K+ channel with an ABC transporter.
AUTHOR: Schwappach B; Zerangue N; Jan Y N; Jan L Y
CORPORATE SOURCE: Department of Physiology, Howard Hughes Medical Institute, University of California, San Francisco 94143, USA.
CONTRACT NUMBER: NS-15963 (NINDS)
SOURCE: NEURON, (2000 Apr) 26 (1) 155-67.
Journal code: AN8; 8809320. ISSN: 0896-6273.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000518
AB K(ATP) channels are large heteromultimeric complexes containing four subunits from the inwardly rectifying K+ channel family (Kir6.2) and four regulatory sulphonylurea receptor subunits from the ATP-**binding** cassette (ABC) transporter family (SUR1 and SUR2A/B). The molecular basis for interactions between these two unrelated protein families is poorly understood. Using novel trafficking-based interaction assays, coimmunoprecipitation, and current measurements, we show that the first transmembrane segment (M1) and the N terminus of Kir6.2 are involved in K(ATP) assembly and gating. Additionally, the transmembrane domains, but not the nucleotide-**binding** domains, of SUR1 are required for interaction with Kir6.2. The identification of specific transmembrane interactions involved in K(ATP) assembly may provide a clue as to how ABC proteins that transport hydrophobic substrates evolved to regulate other membrane proteins.

L5 ANSWER 65 OF 101 MEDLINE DUPLICATE 33
ACCESSION NUMBER: 2000315742 MEDLINE
DOCUMENT NUMBER: 20315742 PubMed ID: 10856718
TITLE: ABC transporters in lipid transport.
AUTHOR: Borst P; Zelcer N; van Helvoort A
CORPORATE SOURCE: Division of Molecular Biology and Centre for Biomedical Genetics, The Netherlands Cancer Institute, Amsterdam.. pborst@nki.nl
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (2000 Jun 26) 1486 (1) 128-44. Ref: 105
Journal code: AOW; 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000810
Last Updated on STN: 20000810
Entered Medline: 20000727

AB Since it was found that the P-glycoproteins encoded by the MDR3 (MDR2) gene in humans and the Mdr2 gene in mice are primarily phosphatidylcholine translocators, there has been increasing interest in the possibility that other ATP **binding** cassette (ABC) transporters are involved in lipid transport. The evidence reviewed here shows that the MDR1 P-glycoprotein and the multidrug resistance (-associated) transporter 1 (MRP1) are able to transport lipid analogues, but probably not major natural membrane lipids. Both transporters can transport a wide range of hydrophobic drugs and may see lipid analogues as just another drug. The MDR3 gene probably arose in evolution from a drug-transporting P-glycoprotein gene. Recent work has shown that the phosphatidylcholine translocator has retained significant drug transport activity and that this transport is **inhibited** by **inhibitors** of drug-transporting P-glycoproteins. Whether the phosphatidylcholine translocator also functions as a transporter of some drugs in vivo remains to be seen. Three other ABC transporters were recently shown to be involved in lipid transport: ABCR, also called Rim protein, was shown to be defective in Stargardt's macular dystrophy; this protein probably transports a complex of retinaldehyde and phosphatidylethanolamine in the retina of the eye. **ABC1** was shown to be essential for the exit of cholesterol from cells and is probably a cholesterol transporter. A third example, the ABC transporter involved in the import of long-chain fatty acids into peroxisomes, is discussed in the chapter by Hettema and Tabak in this volume.

L5 ANSWER 66 OF 101 MEDLINE DUPLICATE 34
ACCESSION NUMBER: 2000246852 MEDLINE
DOCUMENT NUMBER: 20246852 PubMed ID: 10787171
TITLE: Structure and function of apolipoprotein A-I and high-density lipoprotein.
AUTHOR: Segrest J P; Li L; Anantharamaiah G M; Harvey S C; Liadaki K N; Zannis V
CORPORATE SOURCE: Department of Medicine, UAB Medical Center, Birmingham, Alabama 35294-0012, USA.. segrest@uab.edu
CONTRACT NUMBER: HL 34343 (NHLBI)
HL48739 (NHLBI)
SOURCE: CURRENT OPINION IN LIPIDOLOGY, (2000 Apr) 11 (2) 105-15.
Ref: 78
Journal code: B05; 9010000. ISSN: 0957-9672.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20000720
Entered Medline: 20000711
AB Structural biology and molecular modeling have provided intriguing insights into the atomic details of the lipid-associated structure of the major protein component of HDL, apo A-I. For the first time, an atomic resolution map is available for future studies of the molecular interactions of HDL in such biological processes as **ABC1** -regulated HDL assembly, LCAT activation, receptor **binding**, reverse lipid transport and HDL heterogeneity. Within the context of this paradigm, the current review summarizes the state of HDL research.

L5 ANSWER 67 OF 101 MEDLINE DUPLICATE 35
ACCESSION NUMBER: 2000412085 MEDLINE
DOCUMENT NUMBER: 20382730 PubMed ID: 10922475
TITLE: M-ABC2, a new **human** mitochondrial ATP-**binding** cassette membrane protein.
AUTHOR: Zhang F; Hogue D L; Liu L; Fisher C L; Hui D; Childs S; Ling V
CORPORATE SOURCE: BC Cancer Research Centre, British Columbia Cancer Agency, University of British Columbia, 601 West 10th Avenue, V5Z 1L3, Vancouver, BC, Canada.
SOURCE: FEBS LETTERS, (2000 Jul 28) 478 (1-2) 89-94.
Journal code: EUH; 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF218417; GENBANK-AF218418; GENBANK-AF218419
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000829

AB We have isolated a **human** cDNA encoding a novel ATP-**binding** cassette (ABC) protein whose gene was previously localized to chromosome 1q42 [Allikmets et al. (1995) Mamm. Genome 6, 111-117]. The gene transcript is expressed in all **human** tissues examined, with the highest levels in bone marrow. A non-expressed pseudogene also exists at chromosome 15q13-14. The new protein, which is most similar to the mitochondrial (M)-**ABC1** protein, was also localized to mitochondria and therefore designated 'M-ABC2'. The N-terminus of M-ABC2 was shown to contain a mitochondrial-targeting signal sequence.

L5 ANSWER 68 OF 101 MEDLINE DUPLICATE 36
ACCESSION NUMBER: 2000186230 MEDLINE
DOCUMENT NUMBER: 20186230 PubMed ID: 10721452
TITLE: [The best of vascular pathology in 1999]. L'essentiel de 1999 en pathologie vasculaire.
AUTHOR: Emmerich J
CORPORATE SOURCE: Service de medecine vasculaire, Hopital Broussais, Paris.
SOURCE: ARCHIVES DES MALADIES DU COEUR ET DES VAISSEAUX, (2000 Jan) 93 (1 Spec No) 83-6. Ref: 18
Journal code: 7SM; 0406011. ISSN: 0003-9683.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000427
Last Updated on STN: 20000427
Entered Medline: 20000419

AB In vascular pathology, the discovery of the **ABC1** receptor (ATP-**binding**-cassette transporter 1), the deficit of which is responsible for Tangier disease and familial hypoalphalipoproteinaemias, has opened the greatest perspectives with the possibility of new active treatments in the prevention of atherosclerosis. Other advances were more expected. A large British trial convincingly demonstrated that the follow-up of small abdominal aortic aneurysms is reliable. The MEDENOX trial showed the value of prophylaxis of thromboembolic disease in a medical setting and the reduced incidence of phlebographic events. The ICAI study, on the other hand, showed the difficulty of treatment of critical ischaemia of the lower limbs: alprostadil (PGE1) was ineffective with a 6 month follow-up in this pathology. Finally, low dose aspirin is at least as effective as high doses.

L5 ANSWER 69 OF 101 MEDLINE DUPLICATE 37
ACCESSION NUMBER: 2000272802 MEDLINE
DOCUMENT NUMBER: 20272802 PubMed ID: 10812922
TITLE: **ABC1**: the gene for Tangier disease and beyond.
AUTHOR: Ordovas J M
CORPORATE SOURCE: Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA 02111, USA.
SOURCE: NUTRITION REVIEWS, (2000 Mar) 58 (3 Pt 1) 76-9. Ref: 11
Journal code: OAY; 0376405. ISSN: 0029-6643.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000606

AB Coronary heart disease (CHD) is the leading cause of death in America. CHD is multifactorial, and low plasma high-density lipoprotein cholesterol (HDL-C) levels are among the most common biochemical abnormalities observed in CHD patients. The mechanisms controlling plasma HDL-C levels are poorly understood. However, several groups recently reported that mutations at the ATP-**binding** cassette transporter 1 gene (**ABC1**) are responsible for a rare disorder known as Tangier disease, which is characterized in the homozygous state by the virtual absence of circulating plasma HDL. This new finding represents a major breakthrough in our knowledge of lipoprotein metabolism and, more specifically, the reverse cholesterol transport. This information could lead to a more precise assessment of the genetic predisposition to CHD as well as to new therapeutic tools to prevent and treat CHD.

L5 ANSWER 70 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:91481 BIOSIS

DOCUMENT NUMBER: PREV200100091481
TITLE: The metabolic pathways of high-density lipoprotein, low-density lipoprotein, and triglycerides: A current review.
AUTHOR(S): Kwiterovich, Peter O., Jr. (1)
CORPORATE SOURCE: (1) Johns Hopkins Medical Institutions, 550 North Broadway, Suite 308, Baltimore, MD, 21205 USA
SOURCE: American Journal of Cardiology, (December 21, 2000) Vol. 86, No. 12A, pp. 5L-10L. print.
ISSN: 0002-9149.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Three major interconnected pathways are involved in lipoprotein metabolism: (1) the transport of dietary or exogenous fat; (2) the transport of hepatic or endogenous fat; and (3) reverse cholesterol transport. These pathways are interdependent and disruptions in one will affect the function and products of the others. For example, a mutation such as one in the **ABC1** protein can disrupt normal transport and processing of cholesterol. High-density lipoprotein cholesterol (HDL-C) appears to have cardioprotective properties because of its involvement in certain processes such as reverse cholesterol transport and **inhibition** of low-density lipoprotein cholesterol (LDL-C) oxidation. Certain agents, such as niacin, which increases HDL-C, lowers lipoprotein (a), and targets specific enzymes or receptors, may be highly beneficial for patients at risk of cardiovascular disease.

L5 ANSWER 71 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:61097 BIOSIS
DOCUMENT NUMBER: PREV200100061097
TITLE: Localization of **human** ATP-**binding** cassette transporter 1 (**ABC1**) in normal and atherosclerotic tissues by in situ hybridization.
AUTHOR(S): Wilcox, Josiah N. (1); Couse, Tracey L. (1); Wade, David P.; Lawn, Richard M.
CORPORATE SOURCE: (1) Emory Univ, Atlanta, GA USA
SOURCE: Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.282. print.
Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans, Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 72 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:101553 BIOSIS
DOCUMENT NUMBER: PREV200100101553
TITLE: Adenosine triphosphate **binding** cassette transporters **ABC1** and ABC8 modulate the secretion of apolipoprotein E from macrophages.
AUTHOR(S): Von Eckardstein, Arnold (1); Langer, Claus (1); Lorkowski, Stefan (1); Li, Zhengchen (1); Engel, Thomas (1); Cullen, Paul (1); Assmann, Gerd (1)
CORPORATE SOURCE: (1) Univ of Muenster, Muenster Germany
SOURCE: Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.311. print.
Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans, Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 73 OF 101 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:671190 PROMT
TITLE: CV Therapeutics Scientists Demonstrate a Novel Approach to Remove Cholesterol From Cells.
SOURCE: PR Newswire, (14 Oct 1999) pp. 7043.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 843
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Study Finding May Lead to New Treatments for Cholesterol Management to Reduce
THIS IS THE FULL TEXT: COPYRIGHT 1999 PR Newswire Association, Inc.

L5 ANSWER 74 OF 101 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:733538 PROMT
TITLE: CV Therapeutics' Scientist Presents Role of 'Good Cholesterol' Gene At American Heart Association Scientific Sessions.
SOURCE: PR Newswire, (10 Nov 1999) pp. 1876.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 655
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Latest Findings Advance Understanding of Cholesterol Removal Process to Reduce
THIS IS THE FULL TEXT: COPYRIGHT 1999 PR Newswire Association, Inc.

L5 ANSWER 75 OF 101 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:736191 PROMT
TITLE: AMERICAN HEART ASSOCIATION MEETING.
AUTHOR(S): Welch, Mary
SOURCE: BIOWORLD Today, (11 Nov 1999) Vol. 10, No. 216.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 718
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Valentis Inc. said interim Phase II data showed evidence of blood vessel formation when a non-viral vascular endothelial growth factor (VEGF 165) gene medicine was delivered via its cationic lipid gene delivery system.
THIS IS THE FULL TEXT: COPYRIGHT 1999 American Health Consultants, Inc.

Subscription: $1350.00 per year. Published daily (5 times a week). Box 740021, Atlanta, GA 30374.

L5 ANSWER 76 OF 101 MEDLINE DUPLICATE 38
ACCESSION NUMBER: 2000006295 MEDLINE
DOCUMENT NUMBER: 20006295 PubMed ID: 10535983
TITLE: **Human** ATP-**binding** cassette transporter 1 (**ABC1**): genomic organization and identification of the genetic defect in the original Tangier disease kindred.
AUTHOR: Remaley A T; Rust S; Rosier M; Knapper C; Naudin L; Broccardo C; Peterson K M; Koch C; Arnould I; Prades C; Duverger N; Funke H; Assman G; Dinger M; Dean M; Chimini G; Santamarina-Fojo S; Fredrickson D S; Denefle P; Brewer H B Jr
CORPORATE SOURCE: National Institutes of Health, National Heart, Lung and Blood Institute, Bethesda, MD 20892, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Oct 26) 96 (22) 12685-90. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991210

AB Tangier disease is characterized by low serum high density lipoproteins and a biochemical defect in the cellular efflux of lipids to high density lipoproteins. **ABC1**, a member of the ATP-**binding** cassette family, recently has been identified as the defective gene in Tangier disease. We report here the organization of the **human** **ABC1** gene and the identification of a mutation in the **ABC1** gene from the original Tangier disease kindred. The organization of the **human** **ABC1** gene is similar to that of the mouse **ABC1** gene and other related ABC genes. The **ABC1** gene contains 49 exons that range in size from 33 to 249 bp and is over 70 kb in length. Sequence analysis of the **ABC1** gene revealed that the proband for Tangier disease was homozygous for a deletion of nucleotides 3283 and 3284 (TC) in exon 22. The deletion results in a frameshift mutation and a premature stop codon starting at nucleotide 3375. The product is predicted to encode a nonfunctional protein of 1,084 aa, which is approximately half the size of the full-length **ABC1** protein. The loss of a MnlI restriction site, which results from the deletion, was used to establish the genotype of the rest of the kindred. In summary, we report on the genomic organization of the **human** **ABC1**

gene and identify a frameshift mutation in the **ABC1** gene of the index case of Tangier disease. These results will be useful in the future characterization of the structure and function of the **ABC1** gene and the analysis of additional **ABC1** mutations in patients with Tangier disease.

L5 ANSWER 77 OF 101 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:684452 CAPLUS
DOCUMENT NUMBER: 131:349697
TITLE: Effluxed lipids: Tangier Island's latest export
AUTHOR(S): Freeman, Mason W.
CORPORATE SOURCE: Lipid Metabolism Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(20), 10950-10952
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 32 refs. Current findings of Y. Takahashi and J.D. Smith (1999) propose a novel mechanism through which apolipoprotein A-I (apoAI) appears to remove cholesterol from cells, a process that is defective in individuals with Tangier disease. Recently, an ATP **binding** cassette transporter (**ABC1**) was shown to be mutated in patients with Tangier disease. These discoveries and their implications and inter-relationships are discussed.
REFERENCE COUNT: 32
REFERENCE(S): (1) Acton, S; Science 1996, V271, P518 CAPLUS
(2) Allikmets, R; Science 1997, V277, P1805 CAPLUS
(3) Becq, F; J Biol Chem 1997, V272, P2695 CAPLUS
(4) Bodzioch, M; Nat Genet 1999, V22, P347 CAPLUS
(5) Brooks-Wilson, A; Nat Genet 1999, V22, P336 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 78 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:2936 BIOSIS
DOCUMENT NUMBER: PREV200000002936
TITLE: Role of **ABC1** gene in cholesterol efflux and atheroprotection.
AUTHOR(S): Owen, James S. (1)
CORPORATE SOURCE: (1) Department of Medicine, Royal Free and University College Medical School, University College London, London, NW3 2PF UK
SOURCE: Lancet (North American Edition), (Oct. 23, 1999) Vol. 354, No. 9188, pp. 1402-1403.
ISSN: 0099-5355.
DOCUMENT TYPE: Article
LANGUAGE: English

L5 ANSWER 79 OF 101 MEDLINE DUPLICATE 39
ACCESSION NUMBER: 2000001430 MEDLINE
DOCUMENT NUMBER: 20001430 PubMed ID: 10533863
TITLE: Mutations in the **ABC1** gene in familial HDL deficiency with defective cholesterol efflux.
COMMENT: Comment in: Lancet. 1999 Oct 23;354(9188):1402-3
AUTHOR: Marcil M; Brooks-Wilson A; Clee S M; Roomp K; Zhang L H; Yu L; Collins J A; van Dam M; Molhuizen H O; Loubster O; Ouellette B F; Sensen C W; Fichter K; Mott S; Denis M; Boucher B; Pimstone S; Genest J Jr; Kastelein J J; Hayden M R
CORPORATE SOURCE: Xenon Bioresearch Inc, NRC Innovation Centre, Vancouver, British Columbia, Canada.
SOURCE: LANCET, (1999 Oct 16) 354 (9187) 1341-6.
Journal code: L0S; 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000209
Entered Medline: 19991119
AB BACKGROUND: A low concentration of HDL cholesterol is the most common lipoprotein abnormality in patients with premature atherosclerosis. We have shown that Tangier disease, a rare and severe form of HDL deficiency characterised by a biochemical defect in cellular cholesterol efflux, is caused by mutations in the ATP-**binding**-cassette (**ABC1**) gene. This gene codes for the cholesterol-efflux regulatory protein (CERP). We investigated the presence of mutations in this gene in patients

with familial HDL deficiency. METHODS: Three French-Canadian families and one Dutch family with familial HDL deficiency were studied. Fibroblasts from the proband of each family were defective in cellular cholesterol efflux. Genomic DNA of each proband was used for mutation detection with primers flanking each exon of the **ABC1** gene, and for sequencing of the entire coding region of the gene. PCR and restriction-fragment length polymorphism assays specific to each mutation were used to investigate segregation of the mutation in each family, and to test for absence of the mutation in DNA from normal controls. FINDINGS: A different mutation was detected in **ABC1** in each family studied. Each mutation either created a stop codon predicted to result in truncation of CERP, or altered a conserved aminoacid residue. Each mutation segregated with low concentrations of HDL-cholesterol in the family, and was not observed in more than 500 control chromosomes tested. INTERPRETATION: These data show that mutations in **ABC1** are the major cause of familial HDL deficiency associated with defective cholesterol efflux, and that CERP has an essential role in the formation of HDL. Our findings highlight the potential of modulation of **ABC1** as a new route for increasing HDL concentrations.

L5 ANSWER 80 OF 101 MEDLINE
ACCESSION NUMBER: 2000050105 MEDLINE
DOCUMENT NUMBER: 20050105 PubMed ID: 10581369
TITLE: The ABCA subclass of mammalian transporters.
AUTHOR: Broccardo C; Luciani M; Chimini G
CORPORATE SOURCE: Centre d'Immunologie de Marseille-Luminy, Parc Scientifique de Luminy, 13288, Marseille, France.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Dec 6) 1461 (2) 395-404. Ref: 45
Journal code: A0W; 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB We describe here a subclass of mammalian ABC transporters, the ABCA subfamily. This is a unique group that, in contrast to any other **human** ABC transporters, lacks a structural counterpart in yeast. The structural hallmark of the ABCA subfamily is the presence of a stretch of hydrophobic amino acids thought to span the membrane within the putative regulatory (R) domain. As for today, four ABCA transporters have been fully characterised but 11 ABCA-encoding genes have been identified. ABCA-specific motifs in the nucleotide **binding** folds can be detected when analysing the conserved sequences among the different members. These motifs may reveal functional constraints exclusive to this group of ABC transporters.

L5 ANSWER 81 OF 101 MEDLINE DUPLICATE 40
ACCESSION NUMBER: 1999096930 MEDLINE
DOCUMENT NUMBER: 99096930 PubMed ID: 9878413
TITLE: Identification and characterization of a mammalian mitochondrial ATP-**binding** cassette membrane protein.
AUTHOR: Hogue D L; Liu L; Ling V
CORPORATE SOURCE: BC Cancer Research Centre, Vancouver, British Columbia, V5Z 4L3, Canada.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1999 Jan 8) 285 (1) 379-89.
Journal code: J6V; 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF047690
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990311

AB Membrane proteins of the ATP-**binding** cassette (ABC) superfamily are involved in the transport of diverse substrates across organellar and plasma membranes of the mammalian cell. Most **human** ABC proteins identified to date are associated with genetically linked diseases or clinically relevant phenotypes. We describe a new **human** half-molecule ABC protein, designated M-**ABC1**, that contains a predicted single membrane and ATP-**binding** cassette domain. M-

ABC1 is localized to membranes of the mitochondria and its transcript is expressed in all tissues. The N-terminal region of the M-**ABC1** protein was shown to function independently as a mitochondrial signal sequence by its ability to target the green fluorescent protein to the mitochondria. The monomeric 60 kDa M-**ABC1** protein was chemically crosslinked in vivo into a major protein species of 120-130 kDa, thereby confirming that M-**ABC1** exists within a higher ordered ABC protein complex. A dominant negative repression approach using M-**ABC1** protein with site-directed mutations in its Walker A motif revealed that the mutant protein was rapidly degraded and indicated that the intact Walker A motif of M-**ABC1** was required for its stability. The identification of M-**ABC1** extends the known distribution of members of the ABC protein family into the mammalian mitochondrion.

L5 ANSWER 82 OF 101 MEDLINE DUPLICATE 41
ACCESSION NUMBER: 1999364413 MEDLINE
DOCUMENT NUMBER: 99364413 PubMed ID: 10431238
TITLE: Tangier disease is caused by mutations in the gene encoding ATP-**binding** cassette transporter 1.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Rust S; Rosier M; Funke H; Real J; Amoura Z; Piette J C; Deleuze J F; Brewer H B; Duverger N; Denefle P; Assmann G
CORPORATE SOURCE: Institut fur Arteriosklerosеforschung an der Westfalischen Wilhelms-Universitat Munster, Germany.. Rusts@uni-muenster.de
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 352-5. Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF165281; GENBANK-AF165282; GENBANK-AF165283; GENBANK-AF165284; GENBANK-AF165285; GENBANK-AF165286; GENBANK-AF165287; GENBANK-AF165288; GENBANK-AF165289; GENBANK-AF165290; GENBANK-AF165291; GENBANK-AF165292; GENBANK-AF165293; GENBANK-AF165294; GENBANK-AF165295; GENBANK-AF165296; GENBANK-AF165297; GENBANK-AF165298; GENBANK-AF165299; GENBANK-AF165300; GENBANK-AF165301; GENBANK-AF165302; GENBANK-AF165303; GENBANK-AF165304; GENBANK-AF165305; GENBANK-AF165306; GENBANK-AF165307; GENBANK-AF165308; GENBANK-AF165309; GENBANK-AF165310
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Tangier disease (TD) was first discovered nearly 40 years ago in two siblings living on Tangier Island. This autosomal co-dominant condition is characterized in the homozygous state by the absence of HDL-cholesterol (HDL-C) from plasma, hepatosplenomegaly, peripheral neuropathy and frequently premature coronary artery disease (CAD). In heterozygotes, HDL-C levels are about one-half those of normal individuals. Impaired cholesterol efflux from macrophages leads to the presence of foam cells throughout the body, which may explain the increased risk of coronary heart disease in some TD families. We report here refining of our previous linkage of the TD gene to a 1-cM region between markers D9S271 and D9S1866 on chromosome 9q31, in which we found the gene encoding **human** ATP cassette-**binding** transporter 1 (**ABC1**). We also found a change in **ABC1** expression level on cholesterol loading of phorbol ester-treated THP1 macrophages, substantiating the role of **ABC1** in cholesterol efflux. We cloned the full-length cDNA and sequenced the gene in two unrelated families with four TD homozygotes. In the first pedigree, a 1-bp deletion in exon 13, resulting in truncation of the predicted protein to approximately one-fourth of its normal size, co-segregated with the disease phenotype. An in-frame insertion-deletion in exon 12 was found in the second family. Our findings indicate that defects in **ABC1**, encoding a member of the ABC transporter superfamily, are the cause of TD.

L5 ANSWER 83 OF 101 MEDLINE DUPLICATE 42
ACCESSION NUMBER: 1999364412 MEDLINE
DOCUMENT NUMBER: 99364412 PubMed ID: 10431237
TITLE: The gene encoding ATP-**binding** cassette transporter 1 is mutated in Tangier disease.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Bodzioch M; Orso E; Klucken J; Langmann T; Bottcher A; Diederich W; Drobnik W; Barlage S; Buchler C; Porsch-Ozcurumez M; Kaminski W E; Hahmann H W; Oette K;

Rothe G; Aslanidis C; Lackner K J; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Germany.
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 347-51.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Tangier disease (TD) is an autosomal recessive disorder of lipid metabolism. It is characterized by absence of plasma high-density lipoprotein (HDL) and deposition of cholesteryl esters in the reticulo-endothelial system with splenomegaly and enlargement of tonsils and lymph nodes. Although low HDL cholesterol is associated with an increased risk for coronary artery disease, this condition is not consistently found in TD pedigrees. Metabolic studies in TD patients have revealed a rapid catabolism of HDL and its precursors. In contrast to normal mononuclear phagocytes (MNP), MNP from TD individuals degrade internalized HDL in unusual lysosomes, indicating a defect in cellular lipid metabolism. HDL-mediated cholesterol efflux and intracellular lipid trafficking and turnover are abnormal in TD fibroblasts, which have a reduced in vitro growth rate. The TD locus has been mapped to chromosome 9q31. Here we present evidence that TD is caused by mutations in **ABC1**, encoding a member of the ATP-**binding** cassette (ABC) transporter family, located on chromosome 9q22-31. We have analysed five kindreds with TD and identified seven different mutations, including three that are expected to impair the function of the gene product. The identification of **ABC1** as the TD locus has implications for the understanding of cellular HDL metabolism and reverse cholesterol transport, and its association with premature cardiovascular disease.

L5 ANSWER 84 OF 101 MEDLINE DUPLICATE 43
ACCESSION NUMBER: 1999364411 MEDLINE
DOCUMENT NUMBER: 99364411 PubMed ID: 10431236
TITLE: Mutations in **ABC1** in Tangier disease and familial high-density lipoprotein deficiency.
COMMENT: Comment in: Nat Genet. 1999 Aug;22(4):316-8
AUTHOR: Brooks-Wilson A; Marcil M; Clee S M; Zhang L H; Roomp K; van Dam M; Yu L; Brewer C; Collins J A; Molhuizen H O; Loubser O; Ouelette B F; Fichter K; Ashbourne-Excoffon K J; Sensen C W; Scherer S; Mott S; Denis M; Martindale D; Frohlich J; Morgan K; Koop B; Pimstone S; Kastelein J J; Hayden M R; +
CORPORATE SOURCE: Xenon Bioresearch Inc., NRC Innovation Centre, Vancouver, British Columbia, Canada.
SOURCE: NATURE GENETICS, (1999 Aug) 22 (4) 336-45.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376; GENBANK-X75926
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Genes have a major role in the control of high-density lipoprotein (HDL) cholesterol (HDL-C) levels. Here we have identified two Tangier disease (TD) families, confirmed 9q31 linkage and refined the disease locus to a limited genomic region containing the gene encoding the ATP-**binding** cassette transporter (**ABC1**). Familial HDL deficiency (FHA) is a more frequent cause of low HDL levels. On the basis of independent linkage and meiotic recombinants, we localized the FHA locus to the same genomic region as the TD locus. Mutations in **ABC1** were detected in both TD and FHA, indicating that TD and FHA are allelic. This indicates that the protein encoded by **ABC1** is a key gatekeeper influencing intracellular cholesterol transport, hence we have named it cholesterol efflux regulatory protein (CERP).

L5 ANSWER 85 OF 101 MEDLINE DUPLICATE 44
ACCESSION NUMBER: 2000050095 MEDLINE
DOCUMENT NUMBER: 20050095 PubMed ID: 10581359
TITLE: An inventory of the **human** ABC proteins.
AUTHOR: Klein I; Sarkadi B; Varadi A

CORPORATE SOURCE: Institute of Enzymology, Biological Research Center, Hungarian Academy of Sciences, H-1502, Budapest, Hungary.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Dec 6) 1461 (2) 237-62. Ref: 138
Journal code: A0W; 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB Currently 30 **human** ABC proteins are represented by full sequences in various databases, and this paper provides a brief overview of these proteins. ABC proteins are composed of transmembrane domains (TMDs), and nucleotide **binding** domains (NBDs, or ATP-**binding** cassettes, ABSs). The arrangement of these domains, together with available membrane topology models of the family members, are presented. Based on their sequence similarity scores, the members of the **human** ABC protein family can be grouped into eight subfamilies. At present the MDR/TAP, the ALD, the MRP/CFTR, the **ABC1**, the White, the RNAseL **inhibitor**, the ANSA, and the GCN20 subfamilies are identified. Mutations of many **human** ABC proteins are known to be causative in inherited diseases, and a short description of the molecular pathology of these ABC gene-related genetic diseases is also provided.

L5 ANSWER 86 OF 101 MEDLINE DUPLICATE 45
ACCESSION NUMBER: 2000191593 MEDLINE
DOCUMENT NUMBER: 20191593 PubMed ID: 10725792
TITLE: ATP-**binding** cassette transporter A1 (**ABCA1**) in macrophages: a dual function in inflammation and lipid metabolism?.
AUTHOR: Schmitz G; Kaminski W E; Porsch-Ozcurumez M; Klucken J; Orso E; Bodzioch M; Buchler C; Drobnik W
CORPORATE SOURCE: Institute of Clinical Chemistry and Laboratory Medicine, University of Regensburg, Germany.. gerd.schmitz@klinik.uni-regensburg.de
SOURCE: PATHOBIOLOGY, (1999) 67 (5-6) 236-40.
Journal code: AF6; 9007504. ISSN: 1015-2008.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000510

AB Activated lipid-laden macrophages in the vascular wall are key modulators of the inflammatory processes underlying atherosclerosis. We demonstrate here that the ATP-**binding** cassette (ABC) transporter **ABCA1** is induced during differentiation of **human** monocytes into macrophages. **ABCA1** has been implicated in macrophage interleukin-1beta secretion and apoptosis. Moreover, **ABCA1** mRNA and protein levels are strongly upregulated by uptake of modified LDL and downregulated by HDL(3)-mediated lipid efflux in macrophages. Mutation analysis in patients with the classical Tangier disease (TD), a monogenetic disorder characterized by hypersplenism, macrophage accumulation and deposition of cholesteryl esters in the reticuloendothelial system, low plasma HDL and premature atherosclerosis, revealed deleterious mutations in their **ABCA1** gene. The localization pattern of the mutations within the **ABCA1** protein appears to determine the tropism for either the reticuloendothelial system, as seen in the classical TD phenotype, or the artery wall, as in the case of HDL deficiency in the absence of splenomegaly. In a comprehensive analysis of the expression and regulation of all currently known **human** ABC transporters, we identified additional cholesterol-responsive genes that are induced during monocyte differentiation into macrophages. Our results indicate a dual regulatory function for **ABCA1** in macrophage lipid metabolism and inflammation.

L5 ANSWER 87 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:506445 BIOSIS
DOCUMENT NUMBER: PREV199900506445

TITLE: Mutations in transportin (**ABC1**) in Tangier disease and familial HDL deficiency.
AUTHOR(S): Brooks-Wilson, A. R. (1); Marcil, M. (1); Clee, S. M.; Zhang, L.-H. (1); Roomp, K. (1); van Dam, M. J.; Yu, L.; Brewer, C.; Collins, J. A. (1); Molhuizen, H.O.F.; Ouellette, B.F.F.; Sensen, C. W. (1); Martindale, D.; Frohlich, J.; Morgan, K.; Koop, B.; Pimstone, S. (1); Kastelein, J.J.P.; Genest, J., Jr.; Hayden, M. R.
CORPORATE SOURCE: (1) Xenon Bioresearch, Vancouver Canada
SOURCE: American Journal of Human Genetics, (Oct., 1999) Vol. 65, No. 4, pp. A34.
Meeting Info.: 49th Annual Meeting of the American Society of Human Genetics San Francisco, California, USA October 19-23, 1999 The American Society of Human Genetics . ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 88 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:506444 BIOSIS
DOCUMENT NUMBER: PREV199900506444
TITLE: A defective gene associated with atherosclerosis: Tangier disease is caused by mutations in the ATP **binding** cassette transporter 1 (**ABC1**.
AUTHOR(S): Rust, S. (1); Rosier, M.; Funke, H. (1); Real, J.; Amoura, Z.; Piette, J.-C.; Deleuze, J.-F.; Brewer, H. B.; Duverger, N.; Denefle, P.; Assmann, G. (1)
CORPORATE SOURCE: (1) Molecular Genetics, Inst. f. Arteriosclerosis Res., NRW, Muenster Germany
SOURCE: American Journal of Human Genetics, (Oct., 1999) Vol. 65, No. 4, pp. A33.
Meeting Info.: 49th Annual Meeting of the American Society of Human Genetics San Francisco, California, USA October 19-23, 1999 The American Society of Human Genetics . ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 89 OF 101 MEDLINE DUPLICATE 46
ACCESSION NUMBER: 1999194549 MEDLINE
DOCUMENT NUMBER: 99194549 PubMed ID: 10092505
TITLE: Molecular cloning of the **human** ATP-**binding** cassette transporter 1 (hABC1): evidence for sterol-dependent regulation in macrophages.
AUTHOR: Langmann T; Klucken J; Reil M; Liebisch G; Luciani M F; Chimini G; Kaminski W E; Schmitz G
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, 93042, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 Apr 2) 257 (1) 29-33.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ012376
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990511
AB We have cloned the full-length cDNA for the **human** ATP **binding** cassette transporter 1 (hABC1). The 6603-bp open reading frame encodes a polypeptide of 2201 amino acids resulting in a deduced molecular weight of 220 kDa. The hABC1 cDNA is highly homologous (62%) to the **human** rim ABC transporter (ABCR). hABC1 is expressed in a variety of **human** tissues with highest expression levels found in placenta, liver, lung, adrenal glands, and fetal tissues. We demonstrate that the hABC1 expression is induced during differentiation of **human** monocytes into macrophages in vitro. In macrophages, both the hABC1 mRNA and protein expression are upregulated in the presence of acetylated low-density lipoprotein (AcLDL). The AcLDL-induced increase in hABC1 expression is reversed by cholesterol depletion mediated by the addition of high-density lipoprotein (HDL3). Our data, demonstrating sterol-dependent regulation of hABC1 in **human** monocytes/macrophages, suggest a novel role for this transporter molecule in membrane lipid transport.

L5 ANSWER 90 OF 101 MEDLINE DUPLICATE 47

ACCESSION NUMBER: 1998443449 MEDLINE
DOCUMENT NUMBER: 98443449 PubMed ID: 9756759
TITLE: Rapid, transient fluconazole resistance in Candida albicans is associated with increased mRNA levels of CDR.
COMMENT: Erratum in: Antimicrob Agents Chemother 1999 Feb;43(2):438
Erratum in: Rustad T[corrected to Rustad TR]
AUTHOR: Marr K A; Lyons C N; Rustad T R; Bowden R A; White T C; Rustad T
CORPORATE SOURCE: Department of Medicine, University of Washington, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA.. kmarr@u.washington.edu
CONTRACT NUMBER: 2T32 AI108044-21 (NIAID)
CA18029 22 (NCI)
R01 DE11367 (NIDCR)
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1998 Oct) 42 (10) 2584-9.
Journal code: 6HK; 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981109

AB Fluconazole-resistant Candida albicans, a cause of recurrent oropharyngeal candidiasis in patients with **human** immunodeficiency virus infection, has recently emerged as a cause of candidiasis in patients receiving cancer chemotherapy and marrow transplantation (MT). In this study, we performed detailed molecular analyses of a series of C. albicans isolates from an MT patient who developed disseminated candidiasis caused by an azole-resistant strain 2 weeks after initiation of fluconazole prophylaxis (K. A. Marr, T. C. White, J. A. H. vanBurik, and R. A. Bowden, Clin. Infect. Dis. 25:908-910, 1997). DNA sequence analysis of the gene (ERG11) for the azole target enzyme, lanosterol demethylase, revealed no difference between sensitive and resistant isolates. A sterol biosynthesis assay revealed no difference in sterol intermediates between the sensitive and resistant isolates. Northern blotting, performed to quantify mRNA levels of genes encoding enzymes in the ergosterol biosynthesis pathway (ERG7, ERG9, and ERG11) and genes encoding efflux pumps (MDR1, **ABC1**, YCF, and CDR), revealed that azole resistance in this series is associated with increased mRNA levels for members of the ATP **binding** cassette (ABC) transporter superfamily, CDR genes. Serial growth of resistant isolates in azole-free media resulted in an increased susceptibility to azole drugs and corresponding decreased mRNA levels for the CDR genes. These results suggest that C. albicans can become transiently resistant to azole drugs rapidly after exposure to fluconazole, in association with increased expression of ABC transporter efflux pumps.

L5 ANSWER 91 OF 101 MEDLINE DUPLICATE 48
ACCESSION NUMBER: 1998196514 MEDLINE
DOCUMENT NUMBER: 98196514 PubMed ID: 9537224
TITLE: Amplification of the ATP-**binding** cassette 2 transporter gene is functionally linked with enhanced efflux of estramustine in ovarian carcinoma cells.
AUTHOR: Laing N M; Belinsky M G; Kruh G D; Bell D W; Boyd J T; Barone L; Testa J R; Tew K D
CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center, Philadelphia, Pennsylvania 19111, USA.
CONTRACT NUMBER: CA06927 (NCI)
CA53893 (NCI)
RR05539 (NCRR)
SOURCE: CANCER RESEARCH, (1998 Apr 1) 58 (7) 1332-7.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980416

AB An estramustine-resistant **human** ovarian carcinoma cell line, SKEM, was generated to explore resistance mechanisms associated with this agent. Cytogenetic analysis revealed that SKEM cells have a homogeneously staining region (hsr) at chromosome 9q34. Microdissection of the hsr, followed by fluorescence in situ hybridization to SKEM and normal metaphase spreads, confirmed that the amplified region was derived from

sequences from 9q34. In situ hybridization with a probe specific for ABC2, a gene located at 9q34 that encodes an ATP-**binding** cassette 2 (ABC2) transporter, indicated that this gene is amplified approximately 6-fold in the estramustine-resistant cells. Southern analysis confirmed that ABC2 was amplified in SKEM, and Northern analysis indicated that the ABC2 transcript was overexpressed approximately 5-fold. The **ABC1** gene located at 9q22-31 was not amplified in the resistant cells, and mRNA levels of several other ABC transporter genes were unaltered. Consistent with the concept that increased ABC2 expression contributes to the resistant phenotype, we observed that the rate of efflux of dansylated estramustine was increased in SKEM compared with control cells. In addition, antisense treatment directed toward ABC2 mRNA sensitized the resistant cells to estramustine. Together, these results suggest that amplification and overexpression of ABC2 contributes to estramustine resistance and provides the first indication of a potential cellular function for this product.

L5 ANSWER 92 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:98018 BIOSIS
DOCUMENT NUMBER: PREV199900098018
TITLE: Cyclosporines (CS) **inhibit** interleukin-1beta (L-1beta) secretion by the **ABC1** transporter, impair leukemia self-renewal and sensitize AML progenitors to antineoplastics.
AUTHOR(S): List, A. F.; Blinsmann-Gibson, B.; Heaton, R.; Schlegel, S.; Guzman, M.; Futscher, B.
CORPORATE SOURCE: Ariz. Cancer Cent., Univ. Ariz., Tucson, AZ USA
SOURCE: Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2, pp. 675A.
Meeting Info.: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998 The American Society of Heamatology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 93 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:480896 BIOSIS
DOCUMENT NUMBER: PREV199800480896
TITLE: Effect of CRF and related peptides on calcium signaling in **human** and rodent melanoma cells.
AUTHOR(S): Fazal, Nadeem; Slominski, Andrzej (1); Choudhry, Mashkoor A.; Wei, Edward T.; Sayeed, Mohammed M.
CORPORATE SOURCE: (1) Dep. Pathology, Med. Cent., Loyola Univ., 2160 First South Avenue, Maywood, IL 60153 USA
SOURCE: FEBS Letters, (Sept. 18, 1998) Vol. 435, No. 2-3, pp. 187-190.
ISSN: 0014-5793.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Corticotropin releasing factor (CRF) induces a rapid, within seconds, and dose-dependent increase in the intracellular Ca2+ in both **human** and hamster melanoma cells. This effect is **inhibited** by depletion of extracellular calcium using 3 mM EGTA and is attenuated by the CRF receptor antagonist, alpha-helical-CRF(9-41). Other peptides of the CRF superfamily, sauvagine and urocortin, also induce increases in cytoplasmic calcium concentration but at higher concentrations than CRF. We conclude that malignant melanocytes express CRF receptors, which are coupled to activation of plasma membrane calcium channels.

L5 ANSWER 94 OF 101 MEDLINE DUPLICATE 49
ACCESSION NUMBER: 1998332725 MEDLINE
DOCUMENT NUMBER: 98332725 PubMed ID: 9666097
TITLE: Organization of the ABCR gene: analysis of promoter and splice junction sequences.
AUTHOR: Allikmets R; Wasserman W W; Hutchinson A; Smallwood P; Nathans J; Rogan P K; Schneider T D; Dean M
CORPORATE SOURCE: Intramural Research Support Program, SAIC-Frederick, Frederick, MD 21702, USA.
CONTRACT NUMBER: CA74683-02 (NCI)
SOURCE: GENE, (1998 Jul 17) 215 (1) 111-22.
Journal code: FOP; 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917

Entered Medline: 19980904

AB Mutations in the **human** ABCR gene have been associated with the autosomal recessive Stargardt disease (STGD), retinitis pigmentosa (RP19), and cone-rod dystrophy (CRD) and have also been found in a fraction of age-related macular degeneration (AMD) patients. The ABCR gene is a member of the ATP-**binding** cassette (ABC) transporter superfamily and encodes a rod photoreceptor-specific membrane protein. The cytogenetic location of the ABCR gene was refined to 1p22.3-1p22.2. The intron/exon structure was determined for the ABCR gene from overlapping genomic clones. ABCR spans over 100kb and comprises 50 exons. Intron/exon splice site sequences are presented for all exons and analyzed for information content (Ri). Nine splice site sequence variants found in STGD and AMD patients are evaluated as potential mutations. The localization of splice sites reveals a high degree of conservation between other members of the **ABC1** subfamily, e.g. the mouse **Abc1** gene. Analysis of the 870-bp 5' upstream of the transcription start sequence reveals multiple putative photoreceptor-specific regulatory elements including a novel retina-specific transcription factor **binding** site. These results will be useful in further mutational screening of the ABCR gene in various retinopathies and for determining the substrate and/or function of this photoreceptor-specific ABC transporter.

L5 ANSWER 95 OF 101 MEDLINE DUPLICATE 50
ACCESSION NUMBER: 1998025873 MEDLINE
DOCUMENT NUMBER: 98025873 PubMed ID: 9376570
TITLE: Interleukin-1beta secretion is impaired by **inhibitors** of the Atp **binding** cassette transporter, **ABC1**.
AUTHOR: Hamon Y; Luciani M F; Becq F; Verrier B; Rubartelli A; Chimini G
CORPORATE SOURCE: Centre d'Immunologie INSERM-CNRS de Marseille-Luminy, France.
SOURCE: BLOOD, (1997 Oct 15) 90 (8) 2911-5.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 20000303
Entered Medline: 19971112

AB The production of interleukin-1beta (IL-1beta), a powerful mediator of inflammation, is tightly regulated at several levels. However, in some pathologic conditions, a pharmacologic treatment is required to control the toxicity of excessive extracellular IL-1beta. Because of the heavy side effects of most therapies used in IL-1beta-mediated pathologies, a goal of pharmacologic research is the development of selective anti-IL-1beta drugs. We show here that the sulfonylurea glyburide, currently used in the oral therapy of noninsulin dependent diabetes, is an **inhibitor** of IL-1beta secretion from **human** monocytes and mouse macrophages. Glyburide reduces dramatically the recovery of extracellular 17-kD IL-1beta in the absence of toxic effects on the cells and without affecting the synthesis or processing of the IL-1beta precursor. IL-1beta belongs to the family of leaderless secretory proteins released from the cell by a nonclassical secretory route. In bacteria and yeast Atp **binding** cassette (ABC) transporters are involved in the secretion of leaderless secretory proteins. Interestingly, glyburide blocks the anion exchanger function of **ABC1**, a mammalian member of the family of ABC transporters. We thus investigated the involvement of **ABC1** in IL-1beta secretion, through the analysis of the effects of drugs known to **inhibit** IL-1beta secretion, on the activity of **ABC1** and in turn the ability of known **inhibitors** of **ABC1** of blocking IL-1beta secretion. Our data show that IL-1beta secretion and the function of **ABC1** as an anion exchanger are sensitive to the same drugs, therefore suggesting an involvement of the **ABC1** transporter in the secretion of leaderless proteins in mammals.

L5 ANSWER 96 OF 101 MEDLINE
ACCESSION NUMBER: 97160572 MEDLINE
DOCUMENT NUMBER: 97160572 PubMed ID: 9006906
TITLE: **ABC1**, an ATP **binding** cassette transporter required for phagocytosis of apoptotic cells, generates a regulated anion flux after expression in Xenopus laevis oocytes.
AUTHOR: Becq F; Hamon Y; Bajetto A; Gola M; Verrier B; Chimini G
CORPORATE SOURCE: Laboratoire de Neurobiologie Cellulaire, CNRS, 31 Chemin J. Aiguier, 13402 Marseille Cedex 20, France.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jan 31) 272 (5) 2695-9.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X75926
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19980206
Entered Medline: 19970313

AB The ATP **binding** cassette transporter **ABC1** is a 220-kDa glycoprotein expressed by macrophages and required for engulfment of cells undergoing programmed cell death. Since members of this family of proteins such as P-glycoprotein and cystic fibrosis transmembrane conductance regulator share the ability to transport anions, we have investigated the transport capability of **ABC1** expressed in Xenopus oocytes using iodide efflux and voltage-clamp techniques. We report here that **ABC1** generates an anion flux sensitive to glibenclamide, sulfobromophthalein, and blockers of anion transporters. The anion flux generated by **ABC1** is up-regulated by orthovanadate, cAMP, protein kinase A, and okadaic acid. In other ABC transporters, mutating the conserved lysine in the nucleotide **binding** folds was found to severely reduce or abolish hydrolysis of ATP, which in turn altered the activity of the transporter. In **ABC1**, replacement of the conserved lysine 1892 in the Walker A motif of the second nucleotide **binding** fold increased the basal ionic flux, did not alter the pharmacological **inhibitory** profile, but abolished the response to orthovanadate and cAMP agonists. Therefore, we conclude that **ABC1** is a cAMP-dependent and sulfonylurea-sensitive anion transporter.

L5 ANSWER 97 OF 101 MEDLINE DUPLICATE 51
ACCESSION NUMBER: 97179225 MEDLINE
DOCUMENT NUMBER: 97179225 PubMed ID: 9027511
TITLE: The cloning of a **human** ABC gene (ABC3) mapping to chromosome 16p13.3.
AUTHOR: Connors T D; Van Raay T J; Petry L R; Klinger K W; Landes G M; Burn T C
CORPORATE SOURCE: Department of Human Genetics, Genzyme Genetics, Framingham, Massachusetts 01701, USA.
CONTRACT NUMBER: DK44853 (NIDDK)
SOURCE: GENOMICS, (1997 Jan 15) 39 (2) 231-4.
Journal code: GEN; 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U78735
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970331

AB The ATP **binding** cassette (ABC) transporters, or traffic ATPases, constitute a large family of proteins responsible for the transport of a wide variety of substrates across cell membranes in both prokaryotic and eukaryotic cells. We describe a **human** ABC protein with regions of strong homology to the recently described murine **ABC1** and ABC2 transporters. The gene for this novel protein, **human** ABC3, maps near the polycystic kidney disease type 1 (PKD1) gene on chromosome 16p13.3. The ABC3 gene is expressed at highest levels in lung compared to other tissues.

L5 ANSWER 98 OF 101 MEDLINE
ACCESSION NUMBER: 96178218 MEDLINE
DOCUMENT NUMBER: 96178218 PubMed ID: 8617198
TITLE: The ATP **binding** cassette transporter **ABC1** , is required for the engulfment of corpses generated by apoptotic cell death.
AUTHOR: Luciani M F; Chimini G
CORPORATE SOURCE: Centre d'Immunologie INSERM CNRS de Marseille-Luminy, 13288 Marseille Cedex 9, France.
SOURCE: EMBO JOURNAL, (1996 Jan 15) 15 (2) 226-35.
Journal code: EMB; 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960620
Last Updated on STN: 19980206
Entered Medline: 19960613

AB ATP **binding** cassette (ABC) transporters define a family of proteins with strong structural similarities conserved across evolution and devoted to the translocation of a variety of substrates across cell membranes. A few members of the family are known in mammals, but although all of them are medically relevant proteins, knowledge of their molecular function remains scanty. We report here a morphological and functional study of the recently identified mammalian ABC transporter, **ABC1** . Its expression during embryonic development correlates spatially and temporally with the areas of programmed cell death. More specifically, **ABC1** is expressed in macrophages engaged in the engulfment and clearance of dead cells. Moreover, **ABC1** transporter is required for engulfment since the ability of macrophages to ingest apoptotic bodies is severely impaired after antibody-mediated steric blockade of **ABC1**. A structural homologue of **ABC1** has been identified in the Caenorhabditis elegans genome and maps close to the ced-7 locus. Since ced-7 phenotype is precisely defined by an imparied engulfment of cell corpses, it is tempting to surmise that **ABC1** might be a mammalian homologue of ced-7.

L5 ANSWER 99 OF 101 AGRICOLA
ACCESSION NUMBER: 97:24391 AGRICOLA
DOCUMENT NUMBER: IND20556242
TITLE: Cloning by functional complementation, and inactivation, of the Schizosaccharomyces pombe homologue of the Saccharomyces cerevisiae gene **ABC1**.
AUTHOR(S): Bonnefoy, N.; Kermorgant, M.; Brivet-Chevillotte, P.; Dujardin, G.
CORPORATE SOURCE: Laboratoire propre du C.N.R.S., Gif-sur-Yvette, France.
SOURCE: Molecular & general genetics : MGG, May 23, 1996. Vol. 251, No. 2. p. 204-210
Publisher: Berlin, Germany : Springer Produktions-Gesellschaft.
CODEN: MGGEAE; ISSN: 0026-8925
NOTE: Includes references
PUB. COUNTRY: Germany
DOCUMENT TYPE: Article
FILE SEGMENT: Non-U.S. Imprint other than FAO
LANGUAGE: English

AB The Saccharomyces cerevisiae gene **ABC1** is required for the correct functioning of the bc1 complex of the mitochondrial respiratory chain. By functional complementation of a S. cerevisiae **abc1**- mutant, we have cloned a Schizosaccharomyces pombe cDNA, whose predicted product is 50% identical to the **Abc1** protein. Significant homology is also observed with bacterial, nematode, and even **human** amino acid sequences of unknown function, suggesting that the **Abc1** protein is conserved through evolution. The cloned cDNA corresponds to a single S. pombe gene abc1Sp, located on chromosome II, expression of which is not regulated by the carbon source. Inactivation of the abc1Sp gene by homologous gene replacement causes a respiratory deficiency which is efficiently rescued by the expression of the S. cerevisiae **ABC1** gene. The inactivated strain shows a drastic decrease in the bc1 complex activity, a decrease in cytochrome aa3 and a slow growth phenotype. To our knowledge, this is the first example of the inactivation of a respiratory gene in S. pombe. Our results highlight the fact that S. pombe growth is highly dependent upon respiration, and that S. pombe could represent a valuable model for studying nucleo-mitochondrial interactions in higher eukaryotes.

L5 ANSWER 100 OF 101 MEDLINE DUPLICATE 52
ACCESSION NUMBER: 94375008 MEDLINE
DOCUMENT NUMBER: 94375008 PubMed ID: 8088782
TITLE: Cloning of two novel ABC transporters mapping on **human** chromosome 9.
AUTHOR: Luciani M F; Denizot F; Savary S; Mattei M G; Chimini G
CORPORATE SOURCE: Centre d'Immunologie, INSERM-CNRS de Marseille-Luminy, France.
SOURCE: GENOMICS, (1994 May 1) 21 (1) 150-9.
Journal code: GEN; 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X75926; GENBANK-X75927; SWISSPROT-P06795;

SWISSPROT-P08716; SWISSPROT-P21440; SWISSPROT-P21958;
SWISSPROT-P23361; SWISSPROT-P23703
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941031
Last Updated on STN: 19980206
Entered Medline: 19941019

AB The family of ATP **binding** cassette (ABC) transporters or traffic ATPases is composed of several membrane-associated proteins that transport a great variety of solutes across cellular membranes. Two novel mammalian members of the family, **ABC1** and ABC2, have been identified by a PCR-based approach. They belong to a group of traffic ATPases encoded as a single multifunctional protein, such as CFTR, STE 6, and P-glycoproteins. Their peculiar structural features and close relationship to ABC transporters involved in nodulation suggest that **ABC1** and ABC2 define a novel subgroup of mammalian traffic ATPases.

L5 ANSWER 101 OF 101 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:318599 BIOSIS
DOCUMENT NUMBER: PREV199396026949
TITLE: Differential expression of the common beta and specific alpha chains of the receptors for GM-CSF, IL-3, and IL-5 in endothelial cells.
AUTHOR(S): Colotta, F. (1); Bussolino, F.; Polentarutti, N.; Guglielmetti, A.; Sironi, M.; Bocchietto, E.; De Rossi, M.; Mantovani, A.
CORPORATE SOURCE: (1) Ist. Ricerche Farmacol. "Mario Negri", Via Eritrea 62, 20157 Milan Italy
SOURCE: Experimental Cell Research, (1993) Vol. 206, No. 2, pp. 311-317.
ISSN: 0014-4827.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The present study was designed to reexamine the interaction of granulocyte-macrophage colony-stimulating factor (GM-CSF) with endothelial cells (EC) and to investigate the expression of CSF receptor chains in these cells. In agreement with previous data, GM-CSF induced directional migration and, to a lesser degree, proliferation of **human** umbilical vein EC. When compared to basic fibroblast growth factor, GM-CSF was comparable in terms of chemotactic activity and was substantially less active in terms of proliferation. **Binding** studies confirmed the presence of receptors for GM-CSF (GM-CSFR) on EC. The expression of the beta chain common to the GM-CSFR, IL-3 receptor, and IL-5 receptor, as well as of the individual alpha chains, was studied by Northern analysis and/or reverse transcription and polymerase chain reaction. EC expressed high levels of the common beta chain transcripts. Expression of the alpha(GM) and alpha(IL-5) chain mRNA was minimal or absent in normal EC, though the transformed ECV304 endothelial cell line had substantial amounts of alpha(GM) chain mRNA. Unexpectedly, EC expressed alpha(IL-3) chain transcripts. IL-3 induced migration of EC across polycarbonate filters, whereas IL-5 was inactive.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	0	cholesterol adj efflux adj assay	USPAT; EPO; JPO; DERWENT	2001/06/07 08:46
2	L6	176	cholesterol adj transport	USPAT; EPO; JPO; DERWENT	2001/06/07 08:46
3	L11	0	cholesterol adj transport adj assay	USPAT; EPO; JPO; DERWENT	2001/06/07 08:46
4	L16	36	cholesterol adj efflux	USPAT; EPO; JPO; DERWENT	2001/06/07 08:47

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
1	US 6225525 B1	20010501	20	ATP-binding cassette transporter (ABC1) modified transgenic mice	800/18	435/455 ; 435/461 ; 435/463 ; 800/21 ; 800/25 ; 800/9
2	US 6193967 B1	20010227	17	Bispecific reagents for redirected targeting of human lipoproteins	424/136.1	424/143.1 ; 424/145.1 ; 424/158.1 ; 424/178.1
3	US 6156727 A	20001205	32	Anti-atherosclerotic peptides and a transgenic mouse model of antherosclerosis	514/12	530/324
4	US 6139871 A	20001031	26	Liposome compositions and methods for the treatment of atherosclerosis	424/450	428/402.2 ; 514/824
5	US 6080422 A	20000627	44	Methods of angioplasty and cardiac catheterization	424/450	514/77 ; 514/78 ; 514/824
6	US 6079416 A	20000627	46	Method of forcing the reverse transport of cholesterol from a body part to the liver while avoiding harmful disruptions of hepatic cholesterol	128/898	424/450 ; 604/500
7	US 6048903 A	20000411	10	Treatment for blood cholesterol with trans-resveratrol	514/733	514/824

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
8	US 6046166 A	20000404	125	Apolipoprotein A-I agonists and their use to treat dyslipidemic disorders	514/13	435/69.1 ; 514/12 ; 514/2 ; 530/324 ; 530/325 ; 530/326 ; 930/10 ; 930/30
9	US 6037323 A	20000314	125	Apolipoprotein A-I agonists and their use to treat dyslipidemic disorders	514/12	514/13 ; 514/14 ; 514/15 ; 530/324 ; 530/326 ; 530/327 ; 530/328
10	US 6027922 A	20000222	25	Human foam cells and methods for preparing them, monoclonal antibodies to said foam cells and their pharmaceutical and diagnostic use	435/70.21	435/332 ; 435/334 ; 435/343 ; 435/344 ; 435/70.2 ; 436/548 ; 530/387.1 ; 530/387.3 ; 530/388.22 ; 530/388.7 ; 530/388.8 ; 530/809
11	US 6004925 A	19991221	137	Apolipoprotein A-I agonists and their use to treat dyslipidemic disorders	514/2	514/12 ; 514/13 ; 530/300 ; 530/324 ; 530/325 ; 530/326
12	US 6004936 A	19991221	23	Method of use of serum amyloid a protein	514/21	514/12 ; 514/2

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
13	US 5998433 A	19991207	99	Condensed compounds, their production and use	514/301	514/302 ; 540/593 ; 546/114 ; 546/115 ; 546/16 ; 548/453
14	US 5948435 A	19990907	45	Methods of regulating CETP genes, enzymes and other compound, and pharmaceutical composition therefor	424/450	435/91.1
15	US 5922554 A	19990713	30	Inhibition of cellular uptake of cholesterol	435/11	435/4 ; 436/71 ; 552/544
16	US 5877009 A	19990302	73	Isolated ApoA-I gene regulatory sequence elements	435/320.1	536/24.1
17	US 5858400 A	19990112	43	Method of suppressing a rise in LDL concentrations after administration of an agent having small acceptors	424/450	514/824 ; 604/27 ; 604/28
18	US 5854254 A	19981229	38	Male contraceptives	514/277	514/357 ; 514/506 ; 514/646 ; 514/716 ; 514/717 ; 514/718
19	US 5843474 A	19981201	43	Method of dialysis treatment, and dialysis apparatus related thereto	424/450	

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
20	US 5762930 A	19980609	17	Bispecific reagents for redirected targeting of human lipoproteins	424/136.1	424/143.1 ; 424/145.1 ; 424/158.1 ; 424/178.1 ; 435/325 ; 530/387.3 ; 530/388.22 ; 530/388.24 ; 530/388.7
21	US 5746223 A	19980505	45	Method of forcing the reverse transport of cholesterol from a body part to the liver while avoiding harmful disruptions of hepatic cholesterol	128/898	604/522
22	US 5736157 A	19980407	45	Method of regulating cholesterol related genes, enzymes and other compounds, and pharmaceutical compositions	424/450	435/91.1
23	US 5733879 A	19980331	37	Peptides and proteins, process for their preparation and their use as cholesterol acceptors	514/13	514/12 ; 514/21 ; 530/324 ; 530/326 ; 530/359
24	US 5643757 A	19970701	7	High yield production of human apolipoprotein A1 in E. coli.	435/69.7	435/252.33 ; 435/320.1 ; 435/69.6 ; 530/413 ; 530/415
25	US 5318958 A	19940607	11	Amyloid precursor protein	514/21	514/12 ; 514/2

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
26	US 4895558 A	19900123	12	Autologous plasma delipidation using a continuous flow system	604/5.03	210/645 ; 210/651 ; 422/44 ; 604/6.02 ; 604/6.04
27	US 4758581 A	19880719		Pyridyl N-oxides	514/356	546/322
28	US 5318958 A	19940607		Amyloid precursor protein		
29	WO 200078972 A2	20010528		Adenosine triphosphate (ATP) binding cassette (ABC) polynucleotide, useful for the development of agents for the treatment of heart disease and other disorders associated with hypercholesterolemia and [illegible]		
30	WO 200078971 A2	20010528		Adenosine triphosphate (ATP) binding cassette protein (ABC) 1 polynucleotides and polypeptides, useful for treatment of heart disease and other disorders associated with hypercholesterolemia and		

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
31	WO 200078970 A1	20010528		New nucleic acid and proteins from the human ABC1 gene, useful for treating and preventing diseases associated with abnormal reverse transport of cholesterol		
32	US 6004925 A	19991221		Peptide agonists of apolipoprotein A-I		
33	US 6046166 A	20000404		Peptide agonists of apolipoprotein A-I		
34	US 6037323 A	20000314		Peptide agonists of apolipoprotein A-I		
35	WO 9916409 A2	20010430		Nucleic acid encoding apoproteinA-I agonist peptides		
36	US 5733879 A	19980331		New peptide(s) and protein(s) derived from peptide 18A - used for forming complexes with phospho-lipid(s), partic. for treating cardiovascul		

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     (FILE 'HOME' ENTERED AT 08:01:40 ON 07 JUN 2001)

     FILE 'CAPLUS' ENTERED AT 08:02:06 ON 07 JUN 2001
               E HAYDEN MICHAEL R/AU 25
L1             2 S (E3) AND PY<=1999 AND (ATP)
               E WILSON ANGELA R/AU 25
L2             2 S (E3 OR E4) AND PY<=1999
               E PIMSTONE S/AU 25
L3             8 S (E6)

     FILE 'STNGUIDE' ENTERED AT 08:24:57 ON 07 JUN 2001

     FILE 'CAPLUS' ENTERED AT 08:32:15 ON 07 JUN 2001
               E HAYDEN MICHAEL/AU 25
L4            21 S (E3 OR E9) AND PY<=1999 AND (ATP OR CHOLESTEROL OR LIPID OR H

     FILE 'STNGUIDE' ENTERED AT 08:34:12 ON 07 JUN 2001
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=> d ibib abs 1-
YOU HAVE REQUESTED DATA FROM 21 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:782824 CAPLUS
DOCUMENT NUMBER: 132:220845
TITLE: A frequent mutation in the lipoprotein lipase gene (D9N) deteriorates the biochemical and clinical phenotype of familial hypercholesterolemia
AUTHOR(S): Wittekoek, Marianne E.; Moll, Etelka; Pimstone, Simon N.; Trip, Mieke D.; Lansberg, Peter J.; Defesche, Joep C.; Van Doormaal, Jasper J.; **Hayden, Michael R.**; Kastelein, John J. P.
CORPORATE SOURCE: Department of Vascular Medicine, Academic Medical Centre, Amsterdam, 1105 AZ, Neth.
SOURCE: Arterioscler., Thromb., Vasc. Biol. (**1999**), 19(11), 2708-2713
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The D9N substitution is a common mutation in the lipoprotein lipase (LPL) gene. This mutation has been assocd. with reduced levels of **HDL cholesterol** and elevated triglycerides (TG) in a wide variety of patients. The authors investigated the influence of this D9N mutation on **lipid** and lipoprotein levels and risk for cardiovascular disease (CVD) in patients with familial hypercholesterolemia (FH). A total of 2091 FH heterozygotes, all of Dutch extn., were screened for the D9N mutation using std. polymerase chain reaction techniques, followed by specific enzyme digestion. A total of 94 FH subjects carried the D9N mutation at a carrier frequency of 4.5%. Carriers of other common LPL mutations, such as the N291S and the S447X were excluded. Clin. data on 80 FH individuals carrying the D9N were available and were compared with a FH control group matched for age, sex, and body mass index. Anal. revealed significantly higher TG and lower **HDL-cholesterol** levels. Dyslipidemia was more pronounced in D9N carriers with higher body mass index. Moreover, FH patients carrying this common LPL mutation were at higher risk for CVD. The common D9N LPL mutation leads to increased TG and decreased **HDL** plasma levels in patients with FH. These effects are most apparent in those FH heterozygotes with an increased body mass index. Furthermore, this mutation, present in 4.5% of Dutch FH heterozygotes, leads to increased risk for CVD.
REFERENCE COUNT: 30
REFERENCE(S): (3) Burstein, M; J Lipid Res 1970, V11, P583 CAPLUS
(4) Eckel, R; N Engl J Med 1989, V320, P1060 CAPLUS
(6) Fisher, R; J Lipid Res 1995, V36, P2104 CAPLUS
(7) Friedewald, W; Clin Chem 1972, V18, P499 CAPLUS
(8) Gerdes, C; Circulation 1997, V96, P733 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:755246 CAPLUS
DOCUMENT NUMBER: 132:206542
TITLE: Mutations in the ABC1 gene in familial **HDL** deficiency with defective **cholesterol** efflux
AUTHOR(S): Marcil, Michel; Brooks-Wilson, Angela; Clee, Susanne M.; Roomp, Kirsten; Zhang, Lin-Hua; Yu, Lu; Collins, Jennifer A.; Van Dam, Marjel; Molhuizen, Henri O. F.; Loubster, Odell; Ouellette, B. F. Francis; Sensen, Christoph W.; Fichter, Keith; Mott, Stephanie; Denis, Maxime; Boucher, Betsie; Pimstone, Simon; Genest, Jacques, Jr.; Kastelein, John J. P.; **Hayden, Michael R.**
CORPORATE SOURCE: NRC Innovation Centre, Xenon Bioresearch Inc, Vancouver, BC, V5Z 4H4, Can.
SOURCE: Lancet (**1999**), 354(9187), 1341-1346
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background A low concn. of **HDL cholesterol** is the most common lipoprotein abnormality in patients with premature atherosclerosis. The authors have shown that Tangier disease, a rare and severe form of **HDL** deficiency characterized by a biochem. defect in cellular **cholesterol** efflux, is caused by mutations in the **ATP**-binding-cassette (ABC1) gene. This gene codes for the **cholesterol**-efflux regulatory protein (CERP). The authors

investigated the presence of mutations in this gene in patients with familial **HDL** deficiency. Methods Three French-Canadian families and one Dutch family with familial **HDL** deficiency were studied. Fibroblasts from the proband of each family were defective in cellular **cholesterol** efflux. Genomic DNA of each proband was used for mutation detection with primers flanking each exon of the ABC1 gene, and for sequencing of the entire coding region of the gene. PCR and restriction-fragment length polymorphism assays specific to each mutation were used to investigate segregation of the mutation in each family, and to test for absence of the mutation in DNA from normal controls. Findings A different mutation was detected in ABC1 in each family studied. Each mutation either created a stop codon predicted to result in truncation of CERP, or altered a conserved amino-acid residue. Each mutation segregated with low concns. of **HDL-cholesterol** in the family, and was not obsd. in more than 500 control chromosomes tested. Interpretation These data show that mutations in ABC1 are the major cause of familial **HDL** deficiency assocd. with defective **cholesterol** efflux, and that CERP has an essential role in the formation of **HDL**. The authors' findings highlight the potential of modulation of ABC1 as a new route for increasing **HDL** concns.

REFERENCE COUNT: 35
REFERENCE(S):
(1) Allikmets, R; Nat Genet 1997, V15, P236 CAPLUS
(2) Allikmets, R; Science 1997, V277, P1805 CAPLUS
(3) Altschul, S; Nucleic Acids Res 1997, V25, P3389 CAPLUS
(6) Bodzioch, M; Nat Genet 1999, V22, P347 CAPLUS
(8) Brooks-Wilson, A; Nat Genet 1999, V22, P336 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:500259 CAPLUS
DOCUMENT NUMBER: 131:255940
TITLE: Mutations in ABC1 in Tangier disease and familial high-density lipoprotein deficiency
AUTHOR(S): Brooks-Wilson, Angela; Marcil, Michel; Clee, Susanne M.; Zhang, Lin-Hua; Roomp, Kirsten; Van Dam, Marjel; Yu, Lu; Brewer, Carl; Collins, Jennifer A.; Molhuizen, Henri O. F.; Loubser, Odell; Ouelette, B. F. Francis; Fichter, Keith; Ashbourne-Excoffon, Katherine J. D.; Sensen, Christoph W.; Scherer, Stephen; Mott, Stephanie; Denis, Maxime; Martindale, Duane; Frohlich, Jiri; Morgan, Kenneth; Koop, Ben; Pimstone, Simon; Kastelein, John J. P.; Genest, Jacques, Jr.; **Hayden, Michael R.**
CORPORATE SOURCE: NRC Innovation Centre, Xenon Bioresearch Inc., Vancouver, BC, V6T 1W5, Can.
SOURCE: Nat. Genet. (**1999**), 22(4), 336-345
CODEN: NGENEC; ISSN: 1061-4036
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Genes have a major role in the control of high-d. lipoprotein (**HDL**) **cholesterol** (**HDL**-C) levels. Here the authors have identified two Tangier disease (TD) families, confirmed 9q31 linkage and refined the disease locus to a limited genomic region contg. the gene encoding the **ATP**-binding cassette transporter (ABC1). Familial **HDL** deficiency (FHA) is a more frequent cause of low **HDL** levels. On the basis of independent linkage and meiotic recombinants, the authors localized the FHA locus to the same genomic region as the TD locus. Mutations in ABC1 were detected in both TD and FHA, indicating that TD and FHA are allelic. This indicates that the protein encoded by ABC1 is a key gatekeeper influencing intracellular **cholesterol** transport, hence the authors have named it **cholesterol** efflux regulatory protein (CERP).
REFERENCE COUNT: 50
REFERENCE(S):
(1) Allikmets, R; Gene 1998, V215, P111 CAPLUS
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(4) Altschul, S; Nucleic Acids Res 1997, V25, P3389 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:235193 CAPLUS
DOCUMENT NUMBER: 131:30512
TITLE: Lipoprotein lipase activity is decreased in a large

cohort of patients with coronary artery disease and is associated with changes in lipids and lipoproteins

AUTHOR(S): Henderson, Howard E.; Kastelein, John J. P.; Zwinderman, Aeilko H.; Gagne, Eric; Jukema, J. Wouter; Reymer, Paul W. A.; Groenemeyer, Bjorn E.; Lie, Kong I.; Bruschke, Albert V. G.; **Hayden, Michael R.**; Jansen, Hans

CORPORATE SOURCE: Department of Medical Genetics, University of British Columbia, Vancouver, Can.

SOURCE: J. Lipid Res. (**1999**), 40(4), 735-743
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lipoprotein lipase (LPL) is crucial in the hydrolysis of triglycerides (TG) in TG-rich lipoproteins in the formation of **HDL** particles. As both these lipoproteins play an important role in the pathogenesis of atherosclerotic vascular disease, the authors sought to assess the relation between post-heparin LPL (PH-LPL) activity and lipids and lipoproteins in a large, well-defined cohort of Dutch males with coronary artery disease (CAD). These subjects were drawn from the REGRESS study, totaled 730 in no. and were evaluated against 75 healthy, normolipidemic male controls. Fasting mean PH-LPL activity in the CAD subjects was 108 (46) mU/mL, compared to 138 (44) mU/mL in controls. When these patients were divided into activity quartiles, those in the lowest vs. the highest quartile had higher levels of TG, VLDLc (VLDL **cholesterol**) and VLDL-TG. Conversely, levels of TC, LDL, and HDLc were lower in these patients. Also, in this cohort PH-LPL relationships with lipids and lipoproteins were not altered by apoE genotypes. The frequency of common mutations in the LPL gene assocd. with partial LPL deficiency (N291S and D9N carriers) in the lowest quartile for LPL activity was more than double the frequency in the highest quartile (12.0% vs. 5.0%). By contrast, the frequency of the S447X LPL variant rose from 11.5% in the lowest to 18.3% in the highest quartile. This study, in a large cohort of CAD patients, has shown that PH-LPL activity is decreased (22%) when compared to controls; that the D9N and N291S, and S447X LPL variants are genetic determinants, resp., in CAD patients of low and high LPL PH-LPL activities; and that PH-LPL activity is strongly assocd. with changes in lipids and lipoproteins.

REFERENCE COUNT: 61

REFERENCE(S):
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(2) Applebaum-Bowden, D; Arteriosclerosis 1985, V5, P273 CAPLUS
(3) Austin, M; Curr Opin Lipidol 1994, V5, P395 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:539038 CAPLUS
DOCUMENT NUMBER: 129:300593

TITLE: Advances in cardiovascular risk prediction: new biochemical and genetic markers

AUTHOR(S): Ordovas, Jose M.; Cupples, L. Adrienne; Wilson, Peter W. F.; Lahoz, Carlos; Levy, Daniel; Otvos, James D.; McNamara, Judith R.; Gagne, Eric; **Hayden, Michael**; Schaefer, Ernst J.

CORPORATE SOURCE: Lipid Metabolism Laboratory, JM-USDA-HNRCA at Tufts University, Boston, MA, USA

SOURCE: Int. Congr. Ser. (**1998**), 1155(Atherosclerosis XI), 425-431
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion with 26 refs. In clin. practice it is well-accepted that total plasma **cholesterol** is not the best indicator of a patient's risk of coronary heart disease (CHD). Furthermore, study of the established risk factors of high levels of low-d. lipoprotein **cholesterol** (LDL-C) and low levels of high-d. lipoprotein **cholesterol** (**HDL**-C) reveals a considerable overlap between CHD cases and controls. In this report, the authors present some preliminary results showing that lipoprotein remnants detd. using a novel immunochem. technique can potentially improve CHD risk assessment. Moreover, the authors show that NMR spectroscopy could be used to examine the complexity of lipoprotein subclasses and to det. their precise value as CHD risk predictors. This technique allows for high sample throughput and automation; however, this instrumentation is not readily available to small labs. Regarding the use of genetic markers as

CHD risk predictors, it is becoming evident that the apoE gene locus is a major determinant of CHD risk in the population. Moreover, common mutations at the LPL gene locus exert a significant effect on triglyceride and **HDL**-C levels.

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:174062 CAPLUS
DOCUMENT NUMBER: 128:269204
TITLE: A common mutation in the lipoprotein lipase gene (N291S), alters the lipoprotein phenotype and risk for cardiovascular disease in patients with familial hypercholesterolemia
AUTHOR(S): Wittekoek, Marianne E.; Pimstone, Simon N.; Reymer, Paul W. A.; Feuth, Lisette; Botma, Gert-Jan; Defesche, Joep C.; Prins, M.; **Hayden, Michael R.**; Kastelein, John J. P.
CORPORATE SOURCE: Lipid Research Group, Department of Vascular Medicine, Academic Medical Centre, University of Amsterdam, Neth.
SOURCE: Circulation (**1998**), 97(8), 729-735
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recently, a mutation in the lipoprotein lipase (LPL) gene (N291S) has been reported in 2% to 5% of individuals in western populations and is assocd. with increased triglyceride (TG) and reduced **HDL cholesterol** (HDLC) concns. Here the authors report a significant alteration in biochem. and clin. phenotype in subjects with familial hypercholesterolemia (FH) who are heterozygous for this N291S LPL mutation. Sixty-four FH heterozygotes carrying the N291S mutation had a significantly higher TG level, a higher ratio of total **cholesterol** to HDLC, and lower HDLC concns. compared with 175 FH heterozygotes without this LPL mutation. Moreover, the N291S mutation conferred a significantly greater risk for developing cardiovascular disease in FH heterozygotes compared with FH heterozygotes without this LPL mutation (odds ratio, 3.875). These data provide evidence that a common LPL variant (N291S) significantly influences the biochem. phenotype and risk for cardiovascular disease in patients with FH.

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:47071 CAPLUS
DOCUMENT NUMBER: 128:139439
TITLE: Dyslipidemias associated with heterozygous lipoprotein lipase mutations in the French-Canadian population
AUTHOR(S): Julien, Pierre; Gagne, Claude; Ven Murthy, M. R.; Levesque, Georges; Moorjani, Sital; Cadelis, Francois; **Hayden, Michael R.**; Lupien, Paul J.
CORPORATE SOURCE: Department of Medicine, Lipid Research Centre, Laval University Medical Centre, Ste-Foy, G1V 4G2, Can.
SOURCE: Hum. Mutat. (**1998**), (Suppl. 1), S148-S153
CODEN: HUMUE3; ISSN: 1059-7794
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Some 90 adult subjects with heterozygous lipoprotein lipase (LPL) deficiency from 28 French-Canadian families were analyzed. Some 84 individuals carried the previously characterized missense mutation at codon 207, and 6 people carried the previously characterized missense mutation at 188. Heterozygotes for LPL deficiency exhibited familial hypertriglyceridemia with low **HDL** levels and normal LDL levels of apolipoprotein B. All had significantly reduced LPL mass and activity, whereas their hepatic lipase activities were normal. The increased plasma triglycerides were due to increased VLDL triglycerides. Although total plasma **cholesterol** was normal, VLDL **cholesterol** levels were increased. The VLDL **cholesterol**/VLDL triglycerides ratio was significantly reduced. The VLDL apolipoprotein B level was higher in carriers than in noncarriers. The **HDL cholesterol** concn. was decreased, resulting in a higher total **cholesterol**/ **HDL cholesterol** ratio. This decrease in **HDL cholesterol** as well as in **HDL** apolipoprotein A-I was due to significant redn. in the HDL2 fraction. Dyslipoproteinemia (hypertriglyceridemia and hypoalphalipoproteinemia) was more frequently obsd. among carriers than noncarriers.

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:24883 CAPLUS
DOCUMENT NUMBER: 128:123652
TITLE: Correction of hypertriglyceridemia and impaired fat

tolerance in lipoprotein lipase-deficient mice by adenovirus-mediated expression of human lipoprotein lipase

AUTHOR(S): Excoffon, Katherine J. D. Ashbourne; Liu, Guoqing; Miao, Li; Wilson, Janet E.; Mcmanus, Bruce M.; Semenkovich, Clay F.; Coleman, Trey; Benoit, Patrick; Duverger, Nicolas; Branellec, Didier; Denefle, Patrice; **Hayden, Michael R.**; Lewis, M. E. Suzanne

CORPORATE SOURCE: Department of Medical Genetics, University of British Columbia, Vancouver, BC, V6T 1Z4, Can.

SOURCE: Arterioscler., Thromb., Vasc. Biol. (**1997**), 17(11), 2532-2539
CODEN: ATVBFA; ISSN: 1079-5642

PUBLISHER: American Heart Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Humans homozygous or heterozygous for mutations in the lipoprotein lipase (LPL) gene demonstrate significant disturbances in plasma lipoproteins, including raised triglyceride (TG) and reduced **HDL cholesterol** levels. In this study the authors explored the feasibility of adenovirus-mediated gene replacement therapy for LPL deficiency. A total of 5.times.109 plaque-forming units (pfu) of an E1/E3-deleted adenovirus expressing either human LPL (Ad-LPL) or the bacterial .beta.-galactosidase gene (Ad-LacZ) as a control were administered to mice heterozygous for targeted disruption in the LPL gene. Peak expression of total postheparin plasma LPL activity was obsd. at day 7 in Ad-LPL mice vs. Ad-LacZ controls (834 vs. 313 mU/mL), and correlated with human-specific LPL activity (522 mU/mL) and mass (9214 ng/mL), a change that was significant to 14 and 42 days, resp. At day 7, plasma TGs were significantly reduced relative to Ad-LacZ mice (0.17 vs. 1.90 mmol/L) but returned to endogenous levels by day 42. Ectopic liver expression of human LPL was confirmed by in situ hybridization anal. and from raised LPL activity and mass in liver homogenates. Anal. of plasma lipoprotein compn. revealed a marked decrease in VLDL-derived TGs. Severely impaired oral and i.v. fat-load tolerance in LPL-deficient mice was subsequently cor. after Ad-LPL administration and closely paralleled that obsd. in wild-type mice. These findings suggest that liver-targeted, adenovirus-mediated LPL gene transfer offers an effective means for transient correction of altered lipoprotein metab. and impaired fat tolerance due to LPL deficiency.

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:714484 CAPLUS

DOCUMENT NUMBER: 128:22212

TITLE: Relationship between lipoprotein lipase and high density lipoprotein **cholesterol** in mice: modulation by cholesteryl ester transfer protein and dietary status

AUTHOR(S): Clee, Susanne M.; Zhang, Hanfang; Bissada, Nagat; Miao, Li; Ehrenborg, Ewa; Benlian, Pascale; Shen, Garry X.; Angel, Aubie; Leboeuf, Renee C.; **Hayden, Michael R.**

CORPORATE SOURCE: Department of Medical Genetics, University of British Columbia, Vancouver, BC, V6T 1Z4, Can.

SOURCE: J. Lipid Res. (**1997**), 38(10), 2079-2089
CODEN: JLPRAW; ISSN: 0022-2275

PUBLISHER: Lipid Research, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Plasma lipoprotein lipase (LPL) activity correlates with high d. lipoprotein (**HDL**) **cholesterol** levels in humans. However, in several mouse models created either through transgenesis or targeted inactivation of LPL, no significant changes in **HDL cholesterol** values have been evident. One possible explanation for this species difference could be the absence of plasma cholesteryl ester transfer protein (CETP) activity in mice. To explore this possibility and further investigate interactions between LPL and CETP modulating **HDL cholesterol** levels in vivo, we examd. the relationship between LPL activity and **HDL** levels in mice expressing the simian CETP transgene, compared with littermates not carrying the CETP gene. On a chow diet, increasing LPL activity was assocd. with a trend towards increased **HDL** levels (51 .+-. 29 vs. 31 .+-. 4 mg/dL highest vs. lowest tertiles of LPL activity, P = 0.07) in mice expressing CETP, while no such effects were seen in the absence of CETP. Furthermore, in the presence of CETP, a significant pos. correlation between LPL activity and **HDL cholesterol** was evident (r = 0.15, P = 0.006), while in the absence of CETP no such correlation was detected (r = 0.15, P = 0.36), highlighting the

interactions between LPL and CETP in vivo. When mice were challenged with a high fat, high carbohydrate diet, strong correlations between LPL activity and **HDL cholesterol** were seen in both the presence ($r = 0.45$, $P = 0.03$) and absence ($r = 0.73$, $P < 0.001$) of CETP. Therefore, under altered metabolic contexts, such as those induced by dietary challenge, the relation between LPL activity and **HDL cholesterol** may also become evident. Here we have shown that both genetic and environmental factors may modulate the assocn. between LPL activity and **HDL cholesterol**, and provide explanations for the absence of any changes in **HDL** values in mice either transgenic or with targeted disruption of the LPL gene.

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:556980 CAPLUS
Correction of: 1997:437921
DOCUMENT NUMBER: 127:160079
Correction of: 127:93741
TITLE: Genetic variant showing a positive interaction with .beta.-blocking agents with a beneficial influence on lipoprotein lipase activity, **HDL cholesterol**, and triglyceride levels in coronary artery disease patients: the Ser447-stop substitution in the lipoprotein lipase gene
AUTHOR(S): Groenemeijer, Bjorn; Hallman, Michael D.; Reymer, Paul W. A.; Gagne, Eric; Kuivenhoven, Jan Albert; Bruin, Taco; Jansen, Hans; Lie, Kong I.; Bruschke, Albert V. G.; Boerwinkle, Eric; **Hayden, Michael R.**; Kastelein, John J. P.
CORPORATE SOURCE: Dep. Vascular Med., Academic Med. Cent., Amsterdam, 1105 AZ, Neth.
SOURCE: Circulation (**1997**), 95(12), 2628-2635
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lipoprotein lipase (LPL) is the rate-limiting enzyme in the lipolysis of triglyceride-rich lipoproteins, and the gene coding for LPL is therefore a candidate gene in atherogenesis. The authors previously demonstrated that two amino acid substitutions in LPL, the Asn291-Ser and the Asp9-Asn, are assocd. with elevated triglycerides and lower **HDL cholesterol** and are present with greater frequency in coronary artery disease (CAD) patients than in normolipidemic control subjects. Conversely, a third frequent mutation in this gene, the Ser447-stop, is reported by some investigators to underlie higher **HDL cholesterol** levels and would represent a beneficial genetic variant in lipoprotein metab. We therefore sought conclusive evidence for these allegations by investigating the effects of the LPL Ser447-stop mutation on LPL and hepatic lipase (HL) activity, **HDL cholesterol**, and triglycerides in a large group of CAD patients (n=820) with normal to mildly elevated total and LDL **cholesterol** levels. Carriers of the Ser447-stop allele (heterozygotes and homozygotes) had significantly higher postheparin LPL activity (P=.034), normal postheparin HL activity (P=.453), higher **HDL cholesterol** levels (P=.013), and lower triglyceride levels (P=.044) than noncarriers. The influence of the Ser447-stop allele on LPL activity was pronounced in patients using .beta.-blockers (P=.042) and not significant in those not using them (P=.881), suggesting a gene-environment interaction between the Ser447-stop mutation and .beta.-blockers. The authors conclude that the LPL Ser447-stop mutation has a significant pos. effect on LPL activity and **HDL cholesterol** and triglyceride levels and that certain subgroups of CAD patients carrying the Ser447-stop mutation will have less adverse metabolic effects when placed on .beta.-blockers. The LPL Ser447-stop mutation therefore should have a protective effect against the development of atherosclerosis and subsequent CAD.

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:437921 CAPLUS
DOCUMENT NUMBER: 127:93741
TITLE: Genetic variant showing a positive interaction with .beta.-blocking agents with a beneficial influence on lipoprotein lipase activity, **HDL cholesterol**, and triglyceride levels in coronary artery disease patients: the Ser447-stop substitution in the lipoprotein lipase gene
AUTHOR(S): **Hayden, Michael R.**; Kastelein, John J.P.; Reymer, Paul W.A.; Gagne, Eric; Kuivenhoven, Jan Albert; Bruin, Taco; Jansen, Hans; Lie, Kong I.; Bruschke, Albert V.G.; Boerwinkle, Eric

CORPORATE SOURCE: Department of Vascular Medicine, Academic Medical Center, Amsterdam, 1105 AZ, Neth.
SOURCE: Circulation (**1997**), 95(12), 2628-2635
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lipoprotein lipase (LPL) is the rate-limiting enzyme in the lipolysis of triglyceride-rich lipoproteins, and the gene coding for LPL is therefore a candidate gene in atherogenesis. The authors previously demonstrated that two amino acid substitutions in LPL, the Asn291-Ser and the Asp9-Asn, are assocd. with elevated triglycerides and lower **HDL cholesterol** and are present with greater frequency in coronary artery disease (CAD) patients than in normolipidemic control subjects. Conversely, a third frequent mutation in this gene, the Ser447-Stop, is reported by some investigators to underlie higher **HDL cholesterol** levels and would represent a beneficial genetic variant in lipoprotein metab. We therefore sought conclusive evidence for these allegations by investigating the effects of the LPL Ser447-Stop mutation on LPL and hepatic lipase (HL) activity, **HDL cholesterol**, and triglycerides in a large group of CAD patients (n=820) with normal to mildly elevated total and LDL **cholesterol** levels. Carriers of the Ser447-Stop allele (heterozygotes and homozygotes) had significantly higher postheparin LPL activity (P=.034), normal postheparin HL activity (P=.453), higher **HDL cholesterol** levels (P=.013), and lower triglyceride levels (P=.044) than noncarriers. The influence of the Ser447-Stop allele on LPL activity was pronounced in patients using .beta.-blockers (P=.042) and not significant in those not using them (P=.881), suggesting a gene-environment interaction between the Ser447-Stop mutation and .beta.-blockers. The authors conclude that the LPL Ser447-Stop mutation has a significant pos. effect on LPL activity and **HDL cholesterol** and triglyceride levels and that certain subgroups of CAD patients carrying the Ser447-Stop mutation will have less adverse metabolic effects when placed on .beta.-blockers. The LPL Ser447-Stop mutation therefore should have a protective effect against the development of atherosclerosis and subsequent CAD.

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:143925 CAPLUS
DOCUMENT NUMBER: 126:181175
TITLE: Efficient adenovirus-mediated ectopic gene expression of human lipoprotein lipase in human hepatic (HepG2) cells
AUTHOR(S): Liu, Guoqing; Excoffon, Katherine J.D. Ashbourne; Benoit, Patrick; Ginzinger, David G.; Miao, Li; Ehrenborg, Ewa; Duverger, Nicolas; Denefle, Patrice P.; **Hayden, Michael R.**; Lewis, M.E. Suzanne
CORPORATE SOURCE: Department of Medical Genetics, University of British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: Hum. Gene Ther. (**1997**), 8(2), 205-214
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Gene therapy to deliver and express a corrective lipoprotein lipase (LPL) gene may improve the **lipid** profile and reduce the morbidity and potential atherogenic risk from hypertriglyceridemia and dyslipoproteinemia in patients with complete or partial LPL deficiency. The authors have used an E1-/E3-adenoviral vector, with an RSV-driven human LPL cDNA expression cassette (Ad-RSV-LPL), to achieve high ectopic LPL gene expression in the human hepatoma cell line HepG2, an accepted hepatocellular model of lipoprotein metab. Ad-RSV-LPL transduction of HepG2 cells with a multiplicity of infection (moi) between 12.5 and 100 yielded dose-dependent increments in LPL mass and activity. Peak levels of LPL protein of 2,032.1 ng/105 cells per mL (moi 100) correlated with increased activity of 92.7 mU/105 cells per mL relative to negligible LPL levels in Ad-RSV-LacZ (.beta.-galactosidase) controls. Exogenous LPL expression over a 5-day period peaked at day 3. Susceptibility to inhibition by 1 M NaCl and an anti-LPL monoclonal antibody confirmed that lipase activity was indeed derived from human LPL. Hydrolysis, by LPL-overexpressing HepG2 cells, of triglycerides (TG) carried in very-low-d. lipoprotein (VLDL) showed that greater than 50% of the TG disappeared after 4 h of incubation. These results were compatible with FPLC evidence of a marked redn. in VLDL-TG. These results provide strong in vitro evidence that adenoviral-mediated ectopic expression of the human LPL gene could render hepatic cells capable of VLDL catabolism and thus support the possibility for in vivo adenoviral vector-mediated liver-targeted LPL gene therapy.

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:528237 CAPLUS
DOCUMENT NUMBER: 125:218843
TITLE: A frequently occurring mutation in the lipoprotein lipase gene (Asn291Ser) results in altered postprandial chylomicron triglyceride and retinyl palmitate response in normolipidemic carriers
AUTHOR(S): Pimstone, Simon N.; Clee, Susanne M.; Gagne, S. Eric; Miao, Li; Zhang, Hanfang; Stein, Evan A.; **Hayden, Michael R.**
CORPORATE SOURCE: Dep. Med. Genetics, Univ. British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: J. Lipid Res. (**1996**), 37(8), 1675-1684
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An Asn291Ser mutation in exon 6 of the lipoprotein lipase gene (LPL) frequently occurs in Caucasians (2-4%) and results in a partial catalytic defect. Although this mutation may be assocd. with low **HDL cholesterol** and elevated triglyceride levels, some carriers are normolipidemic and may have LPL activity in the normal range in the fasting state. To assess in vivo the influence of dietary stress on the function of this mutation, the authors have performed oral fat load studies on three unrelated normolipidemic Asn291Ser carriers and compared these results to five healthy controls and to a subject with a clear 50% redn. in LPL activity compared with controls. The Asn291Ser carriers exhibited a more pronounced postprandial response compared with non-carriers as evidenced by higher chylomicron triglyceride (TG) and chylomicron retinyl palmitate peaks. Significantly higher area under response curves were also seen for both chylomicron triglycerides and chylomicron retinyl palmitate when compared with non-carriers. These results provide further in vivo evidence for the functional effects of this common mutation despite normal fasting **lipid** levels. These data suggest that even though subjects with this mutation may be normolipidemic in the fasting state, environmental stress such as an oral fat load may unmask the catalytic defect and result in significant disturbances in postprandial chylomicron metab.

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:386040 CAPLUS
DOCUMENT NUMBER: 125:50739
TITLE: Method, reagent and kit for evaluating susceptibility to premature atherosclerosis and its treatment using human lipoprotein lipase gene therapy
INVENTOR(S): **Hayden, Michael R.**; Ma, Yuanhong; Lewis, Suzanne; Liu, Guoquing
PATENT ASSIGNEE(S): University of British Columbia, Can.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9611276	A1	19960418	WO 1995-US13620	19951011	<--
W: CA, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 5658729	A	19970819	US 1994-320604	19941011	<--
CA 2202477	AA	19960418	CA 1995-2202477	19951011	<--
EP 786005	A1	19970730	EP 1995-937598	19951011	<--
R: CH, DE, FR, GB, LI					

PRIORITY APPLN. INFO.: US 1994-320604 19941011
WO 1995-US13620 19951011

AB A single point mutation in the human lipoprotein lipase gene which results in an A .fwdarw. G nucleotide change at codon 291 (nucleotide 1127) of the lipoprotein lipase gene, and a substitution of serine for the normal asparagine in the lipoprotein lipase gene product is seen with increased frequency in patients with coronary artery disease, and is assocd. with an increased susceptibility to coronary artery disease, including in particular premature atherosclerosis. This is expressed as a diminished catalytic activity of lipoprotein lipase, lower **HDL-cholesterol** levels, and higher triglyceride levels. Thus, susceptibility of a human individual to premature atherosclerosis can be evaluated by: (a) obtaining a sample of DNA from the individual; and (b) evaluating the sample of DNA for the presence of nucleotides encoding a serine residue as amino acid 291 of the lipoprotein lipase gene product.

Thus, the mismatched primer 5'-ctgcttcttttggctctgactgta-3' can be used in PCR or strand displacement amplification of the mutant gene region. Patients found to be suffering from or likely to suffer from premature atherosclerosis and other forms of coronary artery disease as a result of a lipoprotein lipase deficiency can be treated using gene therapy. Thus, viral vectors were constructed for gene therapy using an E1 deletion mutant adenovirus, polylysine, and a plasmid contg. human lipoprotein lipase cDNA under control of the cytomegalovirus promoter region. Vectors for introducing human lipoprotein lipase cDNA into mammalian cells were made using the murine leukemia retroviral backbones M3neo, M5neo, and JZen1 which contain long terminal repeat regulatory sequences for the myeloproliferative sarcoma virus. A 1.56-kb DraI-EcoRI fragment encompassing the entire lipase amino acid coding region was subcloned into a unique BamHI site located 3' or 5' to the neomycin phosphotransferase gene. Gene transfer efficiency was up to 57% with an increase in lipoprotein lipase bioactivity up to 14-fold and an increases in enzyme dimer up to 54-fold.

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:975156 CAPLUS
DOCUMENT NUMBER: 124:24804
TITLE: Structural features in lipoprotein lipase necessary for the mediation of lipoprotein uptake into cells
AUTHOR(S): Krapp, Annette; Zhang, Hanfang; Ginzinger, David; Liu, Ming-S; Lindberg, Anna; Olivecrona, Gunilla; **Hayden, Michael R.**; Beisiegel, Ulrike
CORPORATE SOURCE: Med. Klinik, Univ. Krankenhaus Eppendorf, Hamburg, 20246, Germany
SOURCE: J. Lipid Res. (**1995**), 36(11), 2362-73
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lipoprotein lipase (LPL) has been shown to mediate the uptake of lipoproteins into cells. The uptake is initiated by binding of LpL to cell surface proteoglycans and to the low-d. lipoprotein (LDL) receptor-related protein. This ability of LpL is independent of catalytic activity and depends on the intact dimeric structure of the lipase and functional residues in the C-terminal domain. The goal of this study was to identify structural features in human LpL that are essential in mediation of lipoprotein uptake. Naturally occurring variants and LpL mutants produced by site-directed mutagenesis were cloned and expressed in COS cells. A combination of immunoassays and sepn. on heparin-Sepharose columns was used to det. the molar ratio of monomeric to dimeric LpL in the expression media. The mutants were tested for their ability to mediate the uptake of 125I-labeled .beta.-VLDL in cultured Hep3b cells in direct comparison with wild-type LpL. The authors found that the concn. of monomer in the media correlated neg. with the effect on the uptake mediated by the dimeric form of LpL. A mutation affecting the catalytic activity (D156G) resulted in no significant redn. in the lipase-mediated .beta.-VLDL uptake. Point mutations in the proposed **lipid** binding region, W390A or W393A, and the substitution of residues 390-393 with the homologous hepatic lipase (HL) sequence, were also normal, whereas the deletion of residues 390-393 reduced the ability to mediate the uptake by .apprx.60% in comparison to wild-type LPL. A mutation known to impair heparin binding (R294A) was also less efficient than the wild-type enzyme in mediating uptake. In conclusion, it is important to det. the monomer/dimer ratio in mutant prepns. as the presence of monomers inhibits the uptake mediated by dimeric LpL. Moreover, sites involved in heparin and **lipid** binding between residues 390-421 are important for LpL-mediated lipoprotein uptake.

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:952211 CAPLUS
DOCUMENT NUMBER: 124:6383
TITLE: Patients with apoE3 deficiency (E2/2, E3/2, and E4/2) who manifest with hyperlipidemia have increased frequency of an Asn 291 .fwdarw. Ser mutation in the human LPL gene
AUTHOR(S): Zhang, Hanfang; Reymer, Paul W. A.; Liu, Ming-Sun; Forsythe, Ian J.; Groenemeyer, Bjorn E.; Frohlich, Jiri; Brunzell, John D.; Kastelein, John J. P.; **Hayden, Michael R.**; Ma, Yuanhong
CORPORATE SOURCE: Department Medicine, Academic Medical Center, Amsterdam, Neth.
SOURCE: Arterioscler., Thromb., Vasc. Biol. (**1995**), 15(10), 1695-703
CODEN: ATVBFA; ISSN: 1079-5642
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Approx. 1% to 2% of persons in the general population are homozygous for a lipoprotein receptor-binding defective form of apoE (apoE2/2). However, only a small percentage (2% to 5%) of all apoE2/2 homozygotes develop type III hyperlipoproteinemia. Interaction with other genetic and environmental factors are required for the expression of this **lipid** abnormality. The authors sought to investigate the possible role of LPL gene mutations in the development of hyperlipoproteinemia in apoE2/2 homozygotes and in apoE2 heterozygotes. As a first step, the authors performed DNA sequence anal. of all 10 LPL coding exons in 2 patients with the apoE2/2 genotype who had type III hyperlipoproteinemia and identified a single missense mutation (Asn 291.fwdarw.Ser) in exon 6 of the LPL gene. The mutation was then found in 5 of 18 patients with type III hyperlipoproteinemia who had the apoE2/2 genotype (allele frequency = 13.9%; .times. 10-5) and 6 of 22 hyperlipidemic E2 heterozygous patients with the apoE3/2 and E4/2 genotype (allele frequency = 13.6%; .times. 10-5). In contrast, this mutation was found in only 3 of 230 normolipidemic controls (allele frequency = 0.7%). In vitro mutagenesis studies revealed that the Asn 291 .fwdarw. Ser mutant LPL had approx. 60% of LPL catalytic activity and approx. 70% of specific activity compared with wild-type LPL. The heparin binding affinity of the mutant LPL was not impaired. The authors' data suggest that the Asn 291 .fwdarw. Ser substitution is likely to be a significant predisposing factor contributing to the expression of different forms of hyperlipidemia when assocd. with other genetic factors such as the presence of apoE2.

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:366424 CAPLUS
DOCUMENT NUMBER: 122:129780
TITLE: Many roads lead to atheroma
AUTHOR(S): **Hayden, Michael R.**; Reidy, Michael
CORPORATE SOURCE: Department of Medical Genetics, Univ. of British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: Nat. Med. (N. Y.) (**1995**), 1(1), 22-3
CODEN: NAMEFI; ISSN: 1078-8956
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 18 refs. For many years **cholesterol** was seen as the worst enemy of coronary arteries. Recent advances show that interactions between lipoproteins, coagulation and growth factors are important in atherosclerosis.

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:455187 CAPLUS
DOCUMENT NUMBER: 121:55187
TITLE: High frequency of mutations in the human lipoprotein lipase gene in pregnancy-induced chylomicronemia: possible association with apolipoprotein E2 isoform
AUTHOR(S): Ma, Yuanhong; Ooi, Teik C.; Liu, Ming-Sun; Zhang, Hanfang; McPherson, Ruth; Edwards, Alun L.; Forsythe, Ian J.; Frohlich, Jiri; Brunzell, John D.; **Hayden, Michael R.**
CORPORATE SOURCE: Dep. Med., Univ. British Columbia, Vancouver, BC, Can.
SOURCE: J. Lipid Res. (**1994**), 35(6), 1066-75
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Partial deficiency in lipolysis usually results in only mild disturbances of **lipid** levels. However, when this is assocd. with impairment of the uptake of remnant particles and increased prodn. of triglyceride-rich lipoproteins stimulated by environmental factors such as during normal pregnancy, chylomicronemia may ensue. The authors have previously reported a patient who had approx. 12% of normal LPL activity and developed severe chylomicronemia during pregnancy (Ma et al. 1993. J. Clin. Invest. 91: 1953-1958). Here the authors report four new patients with pregnancy-induced chylomicronemia. In the nonpregnant state, these patients had mild to modest elevation of triglyceride levels ranging from 80 to 623 mg/dL (0.9-7.0 mmol/L) but during the third trimester they became severely chylomicronemic with triglyceride levels ranging from 2314 to 14596 mg/dL (26 to 164 mmol/L). Three of these four patients had partial lipoprotein lipase (LPL) deficiency. The mol. characterization of the LPL gene in these three patients with partial LPL deficiency revealed four novel unpublished mutations. Patient #1 is a compd. heterozygote for Leu252Arg and Ala261Thr mutations which are assocd. with 25% of normal LPL activity. In addn., she has an apoE3/2 genotype. Patient #2 is a heterozygote for a Asn291Ser substitution with 69% of LPL activity and also has an apoE3/2 genotype, while patient #3 is a heterozygote for a Trp382Stop mutation with 54% of normal LPL activity and has an apoE4/2 genotype. The fourth patient (#4) with pregnancy-induced chylomicronemia does not have LPL deficiency and has an apoE3/3 genotype. The previously

reported patient (#5) who had 12% of normal LPL activity due to homozygosity for a Ser172Cys mutation also has an E3/3 genotype. The authors' data suggest that mutations in the LPL gene that cause partial LPL deficiency might be a frequency factor in the pathogenesis of pregnancy-induced chylomicronemia.

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:210754 CAPLUS
DOCUMENT NUMBER: 118:210754
TITLE: Genetic and phenotypic heterogeneity in familial lecithin:**cholesterol** acyltransferase (LCAT) deficiency
AUTHOR(S): Funke, Harald; Von Eckardstein, Arnold; Pritchard, P. Haydn; Hornby, Ann E.; Wiebusch, Heiko; Motti, Corradino; **Hayden, Michael R.**; Dachet, Christine; Jacotot, Bernard; et al.
CORPORATE SOURCE: Inst. Atheroscler. Res., Univ. Muenster, Muenster, 4400, Germany
SOURCE: J. Clin. Invest. (**1993**), 91(2), 677-83
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The presence of lecithin:**cholesterol** acyltransferase (LCAT) deficiency in six probands from 5 families originating from 4 different countries was confirmed by the absence or near absence of LCAT activity. Also, other invariate symptoms of LCAT deficiency, a significant increase of unesterified **cholesterol** in plasma lipoproteins and the redn. of plasma **HDL-cholesterol** to levels below one-tenth of normal, were present in all probands. In the probands from two families, no mass was detectable, while in others reduced amts. of LCAT mass indicated the presence of a functionally inactive protein. Sequence anal. identified homozygous missense or nonsense mutations in 4 probands. Two probands from one family both were found to be compd. heterozygotes for a missense mutation and for a single base insertion causing a reading frame-shift. Subsequent family analyses were carried out using mutagenic primers for carrier identification. LCAT activity and LCAT mass in 23 genotypic heterozygotes were approx. half normal and clearly distinct from those of 20 unaffected family members. In the homozygous patients no obvious relationship between residual LCAT activity and the clin. phenotype was seen. The observation that the mol. defects in LCAT deficiency are dispersed in different regions of the enzyme suggests the existence of several functionally important structural domains in this enzyme.

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:568584 CAPLUS
DOCUMENT NUMBER: 117:168584
TITLE: Molecular genetics of human lipoprotein lipase deficiency
AUTHOR(S): **Hayden, Michael R.**; Ma, Yuanhong
CORPORATE SOURCE: Dep. Med. Genet., Univ. British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: Mol. Cell. Biochem. (**1992**), 113(2), 171-6
CODEN: MCBIB8; ISSN: 0300-8177
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 38 refs. Lipoprotein lipase (LPL) hydrolyzes the triglyceride core of circulating chylomicrons and very-low-d. lipoprotein, and modulates the levels and **lipid** compn. of low and high d. lipoproteins. Worldwide, more than 20 mutations in the LPL gene have been identified in patients with familial LPL deficiency. Most of these mutations are clustered in the region encoded by exons 4, 5 and 6 which forms the proposed catalytic domain of LPL. In French Canadians who have the highest reported frequency for LPL deficiency, three common mutations in the LPL gene have been identified which account for approx. 97% of mutant genes in this group. Simple DNA-based tests for the detection of all these mutations have been developed for the screening for carriers of LPL deficiency. This will facilitate further studies of phenotypic expression in heterozygous carriers and assessment of the risk of atherosclerosis in these individuals.

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:487314 CAPLUS
DOCUMENT NUMBER: 109:87314
TITLE: Characterization of six partial deletions in the low-density-lipoprotein (LDL) receptor gene causing familial hypercholesterolemia (FH)
AUTHOR(S): Langlois, Sylvie; Kastelein, Johannes J. P.; **Hayden, Michael R.**

CORPORATE SOURCE: Dep. Med. Genet., Univ. British Columbia, Vancouver, BC, V6T 2B5, Can.
SOURCE: Am. J. Hum. Genet. (**1988**), 43(1), 60-8
CODEN: AJHGAG; ISSN: 0002-9297
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two hundred thirty-four unrelated heterozygotes for familial hypercholesterolemia (FH) were screened to detect major rearrangements in the low-d.-lipoprotein (LDL) receptor gene. Total genomic DNA was analyzed by Southern blot hybridization to probes encompassing exons 1-18 of the LDL receptor gene. Six different mutations were detected and characterized by the use of exon-specific probes and detailed restriction mapping. Each mutation is unique and suggests that mol. heterogeneity underlies the mol. pathol. of FH. There appear to be preferential sites within the LDL receptor gene for major rearrangements resulting in deletions.

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L3 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:167790 CAPLUS
DOCUMENT NUMBER: 134:217169
TITLE: Oxysterols for modulating HDL cholesterol and triglyceride levels by modulating LXR-mediated transcription
INVENTOR(S): Hayden, Michael R.; Brooks-Wilson, Angela R.; **Pimstone, Simon N.**; Clee, Susanne M.
PATENT ASSIGNEE(S): University of British Columbia, Can.; Xenon Genetics, Inc.
SOURCE: PCT Int. Appl., 316 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015676	A2	20010308	WO 2000-IB1492	20000901

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1999-151977 P 19990901
US 2000-526193 A 20000315
US 2000-213958 P 20000623

AB The invention features methods for treating patients having low HDL, a higher than normal triglyceride level, or a cardiovascular disease by administering compds. that modulate ABC1 expression or activity. Compds. of the invention include oxysterols that modulate LXR-mediated transcription.

L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:666871 CAPLUS
DOCUMENT NUMBER: 133:262303
TITLE: Human ABC1 transporter and DNA and methods for modulating cholesterol levels and diagnosing disease
INVENTOR(S): Hayden, Michael R.; Wilson, Angela R.; **Pimstone, Simon N.**
PATENT ASSIGNEE(S): University of British Columbia, Can.; Xenon Bioresearch, Inc.
SOURCE: PCT Int. Appl., 229 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055318	A2	20000921	WO 2000-IB532	20000315
WO 2000055318	A3	20010322		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1100895	A2	20010523	EP 2000-917240	20000315

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:
US 1999-124702 P 19990315
US 1999-138048 P 19990608
US 1999-139600 P 19990617
US 1999-151977 P 19990901
WO 2000-IB532 W 20000315

AB The invention features ABC1 nucleic acids and proteins for the diagnosis and treatment of abnormal cholesterol regulation. The invention also features methods for identifying compds. for modulating cholesterol levels

in an animal (e.g., a human). Thus, ABC transporter gene ABC1 of chromosome 9 has been identified as the gene involved in Tangier disease and familial HDL deficiency. Many polymorphisms, and mutations (deletion, substitution, nonsense, frameshift, and splicing-altering), have been identified. Many of these correlate with disease; some create/delete restriction sites. The cDNA for ABC1 has been cloned and sequenced. The protein encoded by the cDNA has an addnl. 60 amino acids relative to that previously reported: these extra amino acids were shown to be present in vivo and to play an essential part in the activity of the protein. The ABC1 protein has been shown to transport cholesterol. The ABC1 gene was found to have 49 exons. The sequence of each exon with surrounding introns is presented.

L3 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:782824 CAPLUS
DOCUMENT NUMBER: 132:220845
TITLE: A frequent mutation in the lipoprotein lipase gene (D9N) deteriorates the biochemical and clinical phenotype of familial hypercholesterolemia
AUTHOR(S): Wittekoek, Marianne E.; Moll, Etelka; **Pimstone, Simon N.**; Trip, Mieke D.; Lansberg, Peter J.; Defesche, Joep C.; Van Doormaal, Jasper J.; Hayden, Michael R.; Kastelein, John J. P.
CORPORATE SOURCE: Department of Vascular Medicine, Academic Medical Centre, Amsterdam, 1105 AZ, Neth.
SOURCE: Arterioscler., Thromb., Vasc. Biol. (1999), 19(11), 2708-2713
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The D9N substitution is a common mutation in the lipoprotein lipase (LPL) gene. This mutation has been assocd. with reduced levels of HDL cholesterol and elevated triglycerides (TG) in a wide variety of patients. The authors investigated the influence of this D9N mutation on lipid and lipoprotein levels and risk for cardiovascular disease (CVD) in patients with familial hypercholesterolemia (FH). A total of 2091 FH heterozygotes, all of Dutch extn., were screened for the D9N mutation using std. polymerase chain reaction techniques, followed by specific enzyme digestion. A total of 94 FH subjects carried the D9N mutation at a carrier frequency of 4.5%. Carriers of other common LPL mutations, such as the N291S and the S447X were excluded. Clin. data on 80 FH individuals carrying the D9N were available and were compared with a FH control group matched for age, sex, and body mass index. Anal. revealed significantly higher TG and lower HDL-cholesterol levels. Dyslipidemia was more pronounced in D9N carriers with higher body mass index. Moreover, FH patients carrying this common LPL mutation were at higher risk for CVD. The common D9N LPL mutation leads to increased TG and decreased HDL plasma levels in patients with FH. These effects are most apparent in those FH heterozygotes with an increased body mass index. Furthermore, this mutation, present in 4.5% of Dutch FH heterozygotes, leads to increased risk for CVD.
REFERENCE COUNT: 30
REFERENCE(S): (3) Burstein, M; J Lipid Res 1970, V11, P583 CAPLUS
(4) Eckel, R; N Engl J Med 1989, V320, P1060 CAPLUS
(6) Fisher, R; J Lipid Res 1995, V36, P2104 CAPLUS
(7) Friedewald, W; Clin Chem 1972, V18, P499 CAPLUS
(8) Gerdes, C; Circulation 1997, V96, P733 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:174062 CAPLUS
DOCUMENT NUMBER: 128:269204
TITLE: A common mutation in the lipoprotein lipase gene (N291S), alters the lipoprotein phenotype and risk for cardiovascular disease in patients with familial hypercholesterolemia
AUTHOR(S): Wittekoek, Marianne E.; **Pimstone, Simon N.**; Reymer, Paul W. A.; Feuth, Lisette; Botma, Gert-Jan; Defesche, Joep C.; Prins, M.; Hayden, Michael R.; Kastelein, John J. P.
CORPORATE SOURCE: Lipid Research Group, Department of Vascular Medicine, Academic Medical Centre, University of Amsterdam, Neth.
SOURCE: Circulation (1998), 97(8), 729-735
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently, a mutation in the lipoprotein lipase (LPL) gene (N291S) has been reported in 2% to 5% of individuals in western populations and is assocd. with increased triglyceride (TG) and reduced HDL cholesterol (HDLC) concns. Here the authors report a significant alteration in biochem. and clin. phenotype in subjects with familial hypercholesterolemia (FH) who are heterozygous for this N291S LPL mutation. Sixty-four FH heterozygotes carrying the N291S mutation had a significantly higher TG level, a higher ratio of total cholesterol to HDLC, and lower HDLC concns. compared with 175 FH heterozygotes without this LPL mutation. Moreover, the N291S mutation conferred a significantly greater risk for developing cardiovascular disease in FH heterozygotes compared with FH heterozygotes without this LPL mutation (odds ratio, 3.875). These data provide evidence that a common LPL variant (N291S) significantly influences the biochem. phenotype and risk for cardiovascular disease in patients with FH.

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:24892 CAPLUS
DOCUMENT NUMBER: 128:124289
TITLE: Ethnic variation and in vivo effects of the -93t.fwdarw.g promoter variant in the lipoprotein lipase gene
AUTHOR(S): Ehrenborg, Ewa; Clee, Susanne M.; **Pimstone, Simon N.**; Reymer, Paul W. A.; Benlian, Pascale; Hoogendijk, Christiaan F.; Davis, Henry J.; Bissada, Nagat; Miao, Li; Gagne, S. Eric; Greenberg, L. Jacquie; Henry, Ronald; Henderson, Howard; Ordovas, Jose M.; Schaefer, Ernst J.; Kastelein, Johannes J. P.; Kotze, Maritha J.; Hayden, Michael R.
CORPORATE SOURCE: Department of Medical Genetics, University of British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: Arterioscler., Thromb., Vasc. Biol. (1997), 17(11), 2672-2678
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recently, a (t.fwdarw.g) transition at nucleotide -93 in the lipoprotein lipase (LPL) gene promoter has been obsd. in Caucasians. Here, we have compared the frequency of the -93g carriers in three distinct populations (Caucasians, South African Blacks, and Chinese). The carrier frequency in the Caucasian population was 1.7% (4/232), which was in contrast to the South African Black population, which had a frequency for this allele of 76.4% (123/161) of the individuals tested. This transition was not obsd. in the Chinese population under study. Near complete linkage disequil. between the -93g and the previously described D9N mutation was obsd. in the Caucasian population but not in South African Blacks. To further assess the ancestral origins of these DNA changes, DNA haplotyping using a CA repeat 5' to these substitutions was performed. The -93t allele was assocd. with only a few specific dinucleotide repeat sizes. In contrast, the -93g allele occurred on chromosomes with many different repeat lengths. The broad distribution of repeats on -93g carrying chromosomes, their high frequency in the South African Black population, and the conservation of the -93g allele among different species may suggest that the -93g allele is the ancestral allele on which a transition to t and the D9N mutations arose. The very high frequency of the -93g allele distinct from the N9 allele in a cohort of Black South Africans allowed us to specifically assess the phenotypic effects of the -93g allele on lipids. Individuals homozygous for the g allele at -93 showed mildly decreased triglycerides compared with individuals homozygous for the t allele (1.14.+-.0.66 mmol/L vs. 0.82.+-.0.3; P=.04). Thus, the -93g allele in this cohort is assocd. with low plasma triglyceride levels.

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:707094 CAPLUS
DOCUMENT NUMBER: 128:21467
TITLE: Familial defective apolipoprotein B-100 in hypercholesterolemic Chinese Canadians: identification of a unique haplotype of the apolipoprotein B-100 allele
AUTHOR(S): Abdel-Wareth, Laila O.; **Pimstone, Simon N.**; Lagarde, Jean-Pierre; Raisonnier, Alain; Benlian, Pascale; Pritchard, Haydn; Hayden, Michael R.; Frohlich, Jiri J.
CORPORATE SOURCE: Atherosclerosis Specialty Laboratory, Department of Pathology, University of British Colombia, Vancouver, BC, Can.
SOURCE: Atherosclerosis (Shannon, Irel.) (1997), 135(2), 181-185

CODEN: ATHSBL; ISSN: 0021-9150
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Familial defective apo B-100 (FDB) is an autosomal dominant condition resulting in hypercholesterolemia. It is generally obsd. in 1-6% of hypercholesterolemic subjects in Caucasian populations studied. There are, thus far, no reports characterizing the frequency and phenotype of FDB in a Chinese population. The authors report on the frequency of the FDB (Arg(3500).fwdarw.Gln) mutation and the assocd. haplotype among 160 hypercholesterolemic (TC.gtoreq.6.2 mmol/l) Chinese Canadians including 36 subjects with a clin. diagnosis of familial hypercholesterolemia (FH). Screening for the FDB mutation was done using a mutagenic polymerase chain reaction and haplotype anal. was undertaken using eight diallelic markers and the 3'HVR marker. One Chinese Canadian clin. FH heterozygote was pos. for the FDB Arg(3500).fwdarw.Gln mutation while none of the remaining non-FH hypercholesterolemic subjects were carriers of this mutation. Haplotype anal. in the patient pos. for this mutation revealed a unique haplotype which differed from both the common haplotype of this mutation obsd. in Caucasians and from the only other haplotype reported in a Chinese individual. The assocd. haplotype included a 9-base pair deletion in the signal peptide region and the presence of three restriction sites absent in previously reported haplotypes. These data suggest that the apo B-100 Arg(3500).fwdarw.Gln mutation does not appear to be a significant factor contributing to moderate hypercholesterolemia in a Chinese population residing in Canada. However, this mutation was rarely obsd. among Chinese individuals with a clin. diagnosis of FH. The presence among Chinese individuals of two different haplotypes assocd. with this mutation, which are different from what has been described among Caucasians is compatible with multiple recurrent origins for this mutation in the Chinese population.

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:528237 CAPLUS
DOCUMENT NUMBER: 125:218843
TITLE: A frequently occurring mutation in the lipoprotein lipase gene (Asn291Ser) results in altered postprandial chylomicron triglyceride and retinyl palmitate response in normolipidemic carriers
AUTHOR(S): **Pimstone, Simon N.**; Clee, Susanne M.; Gagne, S. Eric; Miao, Li; Zhang, Hanfang; Stein, Evan A.; Hayden, Michael R.
CORPORATE SOURCE: Dep. Med. Genetics, Univ. British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: J. Lipid Res. (1996), 37(8), 1675-1684
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An Asn291Ser mutation in exon 6 of the lipoprotein lipase gene (LPL) frequently occurs in Caucasians (2-4%) and results in a partial catalytic defect. Although this mutation may be assocd. with low HDL cholesterol and elevated triglyceride levels, some carriers are normolipidemic and may have LPL activity in the normal range in the fasting state. To assess in vivo the influence of dietary stress on the function of this mutation, the authors have performed oral fat load studies on three unrelated normolipidemic Asn291Ser carriers and compared these results to five healthy controls and to a subject with a clear 50% redn. in LPL activity compared with controls. The Asn291Ser carriers exhibited a more pronounced postprandial response compared with non-carriers as evidenced by higher chylomicron triglyceride (TG) and chylomicron retinyl palmitate peaks. Significantly higher area under response curves were also seen for both chylomicron triglycerides and chylomicron retinyl palmitate when compared with non-carriers. These results provide further in vivo evidence for the functional effects of this common mutation despite normal fasting lipid levels. These data suggest that even though subjects with this mutation may be normolipidemic in the fasting state, environmental stress such as an oral fat load may unmask the catalytic defect and result in significant disturbances in postprandial chylomicron metab.

L3 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:952212 CAPLUS
DOCUMENT NUMBER: 124:6384
TITLE: Mutations in the gene for lipoprotein lipase: A cause for low HDL cholesterol levels in individuals heterozygous for familial hypercholesterolemia
AUTHOR(S): **Pimstone, Simon N.**; Gagne, S. Eric; Gagne, Claude; Lupien, Paul J.; Gaudet, Daniel; Williams, Roger R.; Kotze, Maritha; Reymer, Paul W. A.; Defesche, Joep C.; et al.

CORPORATE SOURCE: Department Medical Genetics, University British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: Arterioscler., Thromb., Vasc. Biol. (1995), 15(10), 1704-12
CODEN: ATVBFA; ISSN: 1079-5642
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Familial hypercholesterolemia (FH) is characterized by elevated plasma concns. of LDL cholesterol resulting from mutations in the gene for the LDL receptor. Low HDL cholesterol levels are seen frequently in patients both heterozygous and homozygous for mutations in this gene. Suggested mechanisms for reduced HDL levels in FH patients have been altered apolipoprotein A-1 metab. and elevated cholesteryl ester transfer protein activity, but the mol. basis for hypoalphalipoproteinemia in any of these patients has not yet been identified. The authors investigated four large families in which individuals were double heterozygotes for both FH and lipoprotein lipase (LPL) deficiency. These double heterozygotes have significantly less HDL cholesterol than persons with FH or LPL heterozygosity alone. In the double heterozygotes, HDL particle compn. is not significantly different from FH heterozygotes, suggesting a quant. rather than qual. defect in HDL metab. in these persons. The authors propose that mutations in the LPL gene may be a cause of low HDL cholesterol levels in some individuals heterozygous for FH.

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:378566 CAPLUS
DOCUMENT NUMBER: 122:179825
TITLE: Physical mapping of a 2-Mb region centered at D10S94, a locus very tightly linked to the multiple endocrine neoplasia type 2 gene(s)
AUTHOR(S): **Wilson, Angela Ruth**
CORPORATE SOURCE: Univ. British Columbia (Canada), Vancouver, BC, Can.
SOURCE: (**1993**) 154 pp. Avail.: NLC Order No. DANN85508
From: Diss. Abstr. Int. B 1994, 55(3), 696-7
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:129749 CAPLUS
DOCUMENT NUMBER: 118:129749
TITLE: Ultramicrotomy: a unique method for preparation of composite solder for transmission electron microscopy
AUTHOR(S): Jacobs, Elizabeth G.; Foster, L. Ann; Wu, Yujing; **Wilson, Angela R.**; Pinizzotto, Russell F.
CORPORATE SOURCE: Cent. Mater. Charact., Univ. North Texas, Denton, TX, 76203-5308, USA
SOURCE: J. Mater. Res. (**1993**), 8(1), 87-94
CODEN: JMREEE; ISSN: 0884-2914
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ultramicrotomy was successfully implemented for sectioning solder/Cu and composite solder/Cu samples for TEM. Solder/Cu joints, approx. 10 mm by 2 mm by 3 mm, were C-coated and dipped in cyanoacrylate ester before being embedded into an epoxy mount. The mounted samples were trimmed in a series of steps to obtain a pyramid-shaped, embedded sample with a flat, trapezoidal face of exposed metal for sectioning. Thin sections were sliced directly from the bulk sample using an ultramicrotome and a diamond knife. Once sectioned, the samples were placed on Formvar and C-coated Cu grids for examn. by TEM. Solder/Cu joints made with eutectic (63Sn/37Pb) solder and several composite solders which included Cu and Cu6Sn5 particles were examd. For the first time, it was possible to image simultaneously each phase in the material using a single TEM sample. The various phases present in the solder joints, including the Pb-rich and Sn-rich solder phases, the Cu6Sn5 and Cu3Sn intermetallic phases, and Cu were identified using selected are electron diffraction. Artifacts due to sectioning, such as knife marks, intermetallic tearing, and brittle phase extn., were obsd. These artifacts were minimized by controlling the sectioning conditions.